RESEARCH

BLADDER PRESERVATION WITH IMAGE-GUIDED RADIOTHERAPY FOR ELDERLY PATIENTS WITH MUSCLE-INVASIVE BLADDER CANCER: A SINGLE INSTUTION EXPERIENCE

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2021.213
2021; 24(2): 174-184

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Received: Mar 04, 2021
Accepted: May 16, 2021

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Abstract

Introduction: The number of elderly patients with bladder cancer is expected to triple in the coming years in proportion to the increasing elderly population in the world. The aim of this study was to identify the prognostic factors affecting survival among elderly patients undergoing chemoradiotherapy for muscle-invasive bladder cancer.

Materials and Method: We retrospectively reviewed medical records from 93 biopsy-proven nonmetastatic elderly patients with bladder cancer ≥ 65 years who were treated with helical tomotherapy. The patients received 64.8 Gy to the bladder with concurrent intravenous cisplatin (40 mg/m2) chemotherapy weekly as a radiosensitizer.

Results: The mean follow-up time was 34.1 months (range, 4.0–99.1 months). The two- and five-year overall survival, disease-free survival, and cancer-specific survival rates were 70.6%, and 36.9%, 50.6% and 28.5%, 89.1%, and 58.5%, respectively. Multivariate analysis indicated that urothelial obstruction was an independent prognostic factor affecting survival rates. No grade 4 adverse events and deaths attributable to treatment occurred during chemoradiotherapy

Conclusion: Image guided radiotherapy with chemotherapy as a bladder-sparing approach is a tolerable alternative therapeutic option without severe acute and late toxicities in elderly patients who are unfit for radical cystectomy or refuse surgery.

Keywords: Radiotherapy, Image-Guided; Chemoradiotherapy; Urinary Bladder Neoplasms

INTRODUCTION

Bladder cancer (BC) represents about 5%–10% of male cancers in Europe and United States and is the fourth most common cancer in men in the western world after prostate, lung, and colon cancers (1). Tobacco smoking and occupational exposure to aromatic amines are the most commonly accepted risk factors for BC. Age, stage, and gender are also the main recognized factors affecting the survival and prognosis of patients with BC (2).

BCs are often classified as non-muscle invasive, muscle-invasive, or metastatic. If left untreated, muscle-invasive bladder cancer (MIBC) is potentially lethal, with a five-year survival rate of ?15%. The mainstay treatment for MIBC is radical cystectomy and bilateral pelvic lymph node dissection with neoadjuvant cisplatin-based chemotherapy (3).

In recent years, there has been an increasing trend for organ-preserving approaches across multiple cancer types (e.g., breast, kidney, prostate, anal, and laryngeal cancers). This trend includes the development of various strategies involving definitive non-cystectomy surgical resection in combination with chemotherapy and radiation therapy (RT), which achieves five-year survival rates of 50%–60% and maintains an intact bladder in over 70% of patients (4). Although RT alone is a method of bladder preservation, the treatment response is lower at 56%; there is also a relatively high rate of local recurrence or persistence that can lead to a need for salvage cystectomy (5).

The addition of chemotherapy to RT resulted in improved local control, good long-term bladder function, and a reduced rate of the need for cystectomy (6). Based on data from trials, RT alone has been avoided in cases who can tolerate concurrent chemoradiotherapy (CRT). However, concomitant therapy may be more challenging due to the severe hemotologic and renal toxicities. Bladder-preservation strategies are attractive for elderly patients with greater comorbidities who are not candidates for surgery (7), but it is also known that these patients cannot tolerate most chemotherapy regimens. In this study, we aimed to identify the prognostic factors affecting survival among elderly patients undergoing chemoradiotherapy for muscle-invasive bladder cancer.

MATERIALS AND METHOD

The current study protocol was approved by the Ethics Committee in our hospital. Data from 93 patients with biopsy-confirmed MIBC who underwent concurrent CRT between January 2011 and December 2018 at our Radiation Oncology Department were retrospectively reviewed. All the involved patients included either rejected surgery or were not suitable for surgery due to comorbidities. Table 1 shows the patient and tumor characteristics.

Cystoscopic evolution with transurethral resection (TUR) was applied prior to CRT. The American Joint Committee on Cancer 7th edition 2010 TNM staging system was used as a reference for tumor staging. Computed tomography (CT) and magnetic resonance imaging (MRI) were used to detect intrapelvic and regional lymph nodes.

CRT

RT was performed by a tomotherapy accelerator using 6 MV photons and delivering a median total dose of 64.8 Gy (range, 40.6–66.6) in a 1.8 Gy/fraction. Daily megavoltage computed tomography was acquired for patient positioning. Clinical target volume encompassed the urinary bladder, which was identified on contrast-enhanced CT or MRI with a 2 cm margin. In each fraction, an empty bladder was compulsory. Cisplatin at 40 mg/m^2/week was started on day 1 and given within 60 minutes of IV infusion, which was continued weekly until the last week.

Total blood counts and kidney function tests were performed weekly, and chemotherapy dose reduction was applied when ≥ grade 3 hemotologic and renal toxicities were experienced

Table 1. Patient and tumor characteristics

Characteristic		n (%)
Gender		
	Male	84 (90.3)
	Female	9 (9.7)
Age (years)		
	Mean ± SD	73.86 ±9.1
	Range	44-91
Tumor size (cm)		
	≤5	46 (49.5)
	>5	18 (19.4)
	Unknown	29 (31.1)
Procedure		
	Complete TUR	29 (31.9)
	Incomplete TUR	62 (68.1)
Histopathological type		
	LGPUC	6 (6.5)
	HGPUC	72 (77.4)
	Mixt, Other	15 (16.1)
T Stage		
	I	4 (4.3)
	II	70 (75.3)
	IIIa	9 (9.7)
	IIIb	-
	IVa	10 (10.7)
Node Status		
	N0	80 (89.9)
	N1-2	9 (10.1)
Grade		
	I- II	6 (6.5)
	III-IV	87 (93.5)
Urothelial obstruction		
	No	76 (82.6)
	Yes	16 (17.4)

Abbreviations:TUR=transurethral resection of the bladder, HGPUC= high-grade papillary urothelial carcinoma, LGPUC= low-grade papillary urothelial carcinoma; Mixt = adenosquamos; Other = Squamos, adeno cancer, undifferentiated carcinoma, small cell carcinoma.

Evaluation and follow-up

Tumor response was assessed through a combination of cystoscopy and CT four to six weeks after finishing treatment. Subsequent radiologic and cystoscopic follow-up was performed once every three months for two years and then once every six months.

Statistical analysis

The analysis was performed using SPSS version 13 software. Overall survival (OS) was calculated from the completion of CRT to the date of death or last follow-up. Disease-free survival (DFS) was defined as the time from the completion of CRT to the date of local recurrence or progression. Cancer-specific survival (CSS) was documented as the time from completion of CRT to death due to disease.

Kaplan–Meier survival analysis was used to examine the distribution of survival times. A Log-rank test was used to determine the difference in survival between the groups. Bonferroni correction was applied in the comparisons between the groups. In the multivariate analysis, independent predictors of survival were examined using Cox regression analysis. Chi-square and Fisher's exact test were used to determine the factors influencing treatment response. Cases below 5% of type-1 error levels were accepted as statistically significant.

RESULTS

Patients and tumor characteristics

A total of 93 patients were included in this study. The mean follow-up time was 34.1 months (range, 4.0–99.1 months). By the end of the follow-up period, 39 patients were still alive while 54 had died. The median age of patients was 75 years (range, 44–91). Data showed a clear male preponderance of approximately 9.3:1. Overall, 77.4% of the patients had high-grade disease. About 32% of the patients

had undergone complete TUR, and 68% underwent incomplete TUR. Table 1 summarizes the patient characteristics.

Proportional hazards analysis

Multivariate and univariate analyses were used to provide quantitative estimates of the association of the following 10 clinical and pathological tumor factors with OS, DFS, and CSS in the 93 patients studied: age (<70 and >70), gender, tumor histology, tumor size (5 cm and >5 cm), tumor grade (good, medium, and poor or undifferentiated), T stage (1, 2, and 3–4), nodal status, urothelial obstruction, initial TUR procedure (complete or incomplete), and treatment response.

The results of univariate analysis to determine the prognostic factors showed that urothelial obstruction (P = 0.013) and treatment response (p<0.001) had significant effects on OS. TUR procedure (P = 0.062) was closely significant (Table 2). The multivariate analysis revealed a significant relationship between urothelial obstruction and OS (hazard ratio [HR]: 1.5; 95% CI: 3.6 (1.4–9.3); P=0.007) (Table 3).

Urothelial obstruction (P = 0.038), TUR procedure (P = 0.047) and treatment response (p<0.001) had significant effects on DFS in the univariate analysis (Table 4). The multivariate analysis indicated that urothelial obstruction (HR: 1.5; 95% CI: 5.6 (1.8–17.3); P=0.003) was significant (Table 3).

From univariate analyses, the variables determined as statistically significant prognostic factors on CSS included urothelial obstruction (p < 0.001) and treatment response (P = 0.001) (Table 5). Multivariate analysis indicated that urothelial obstruction (HR: 1.5; 95% CI: 2.7 (1.1–6.5); P=0.031) was significant (Table 3).

Overall Survival

The median OS was 36.6 months (%95 GI: 19.6–53.7). The two- and five-year OS rates were 70.6% and 36.9%, respectively (Figure 1). The overall actuarial survival was significantly better among the 60 patients with complete responses than among the 25 with incomplete responses to the CRT. The five-year OS rate was 49.1% for patients with complete responses but dropped to 10.6% for patients with incomplete responses (p < 0.001). The 76 patients who did not have urothelial obstruction at presentation had significantly better OS. The two-year OS rate was 74.4% for patients without urothelial obstruction at presentation but dropped to 57.4% for patients with urothelial obstruction (P = 0.007).

Disease-Free Survival

The median DFS was 24.5 months (%95 CI: 14.5–34.6). The two- and five-year DFS rates were 50.6% and 28.5%, respectively. The 29 patients with initial complete TUR had significantly better DFS than did the 62 with incomplete TUR. The five-year DFS rate was 50.7% for patients who underwent complete TUR but dropped to 20.9% for patients with complete TUR (P = 0.047). The overall actuarial survival was significantly better among the 60 patients with complete responses than among the 25 with incomplete responses to the CRT. The five-year DFS rate was 39% for patients with complete responses but dropped to 6.4% for patients with incomplete responses (p < 0.001). OS was significantly better among the 76 patients who did not have urothelial obstruction at presentation. The two-year DFS rate was 54.3% for patients without urothelial obstruction at presentation but dropped to 36.5% for patients with urothelial obstruction (P = 0.038).

Cancer-Specific Survival

The median CSS was 69.3 months (%95 CI: 39.6–99). The two- and five-year CSS rates were 89.1% and 59.5%, respectively. The overall actuarial survival among the 60 patients with complete responses was significantly better than among the 25 with incomplete responses to the CRT. The five-year CSS

Table 2. Results of log-rank univariate analysis for overall survival

Variable	n	Median Survival (95% CI)	2-y OS (%) (±SE)	5-y OS (%) (±SE)	p value
Age (year)					
<70	23	57.4 (38.8-76.0)	74.8 (±0.11)	58.2 (±0.14)	0.345
70≤	70	46.3 (38.1-54.5)	69.7 (±0.06)	32.4 (±0.07)	
Gender					
Male	84	36.6 (21.6-51.7)	71.5 (±0.05)	38.5 (±0.07)	0.363
Female	9	24.5 (19.0-30.1)	62.5 (±0.17)	25 (±0.15)	
Tumor diameter (cm)					
≤5	46	55.2 (15.2-95.3)	74 (±0.07)	46.6 (±0.09)	0.455
> 5	18	33.5 (13.8-53.3)	75 (±0.11)	32.1 (±0.13)	
Tumor histologic					
LGPUC	6	54.4 (2.5-106.3)	66.7 (±0.19)	50 (±0.20)	0.305
HGPUC	72	33.5 (26.9-40.2)	69.5 (±0.06)	30.7 (±0.07)	
Mixt, Other	15	67.9 (0-136.9)	76.9 (±0.12)	52.7 (±0.14)	
Histologic grade					
G1-G2	6	54.4 (2.5-106.3)	66.7 (±0.19)	50 (±0.20)	0.835
G3-G4	87	34.4 (23.2-45.6)	70.9 (±0.05)	35.8 (±0.06)	
T Stage					
T1	4	17.9 (6.8-29.1)	33.3 (±0.27)	33.3 (±0.27)	0.878
T2	70	36.6 (18.2-55.1)	70.6 (±0.06)	39.5 (±0.07)	
T3-4	19	33.5 (0-72.9)	76.5 (±0.10)	27.9 (±0.13)	
Node Status					
N0	80	40.4 (23.2-57.5)	73.8 (±0.05)	38.4 (±0.07)	0.511
N1-2	9	29.6 (0.2-59.1)	66.7 (±0.16)	22.2 (±0.19)	
Urothelial obstruction					
No	76	49.9 (29.9-69.9)	74.4 (±0.05)	42.9 (±0.07)	0.013
Yes	16	29.6 (16.6-42.7)	57.4 (±0.13)	0	
Procedure					
Complete TUR	29	65.1 (31.3-98.8)	79.1 (±0.08)	54.1 (±0.12)	0.075
Incomplete TUR	62	29.6 (22.4-36.9)	67.9 (±0.06)	30.5 (±0.07)	
Treatment response					
No	25	24.5 (12.6-36.5)	50.1 (±0.10)	10.6 (±0.09)	<0.001
Yes	60	55.2 (36.5-73.9)	81.3 (±0.05)	49.1 (±0.08)	

Abbreviations: TUR=transurethral resection of the bladder, HGPUC=high-grade papillary urothelial carcinoma, LGPUC= low-grade papillary urothelial carcinoma.

Table 3. Results of multivariate analysis for overall survival, cause-specific survival and disease-free survival by Cox proportional hazard model

Variable	Overall survival		Cause-specific survival		Disease-free survival	
	Hazard Ratio (95% CI)	p value	Hazard Ratio (95% CI)	p value	Hazard Ratio (95% CI)	p value
Age (year)						
<70 vs 70≤	1.9 (0.6-5.3)	0.255	1.1 (0.3-4.2)	0.851	1.3 (0.5-3.3)	0.542
Gender						
Male vs Female	0.8 (0.2-2.6)	0.665	2.2 (0.6-8.6)	0.247	0.8 (0.2-2.7)	0.677
Tumor diameter (cm)						
5≤ vs >5	1.0 (0.4-2.4)	0.990	0.9 (0.3-2.8)	0.894	0.9 (0.4-2.1)	0.778
Tumor histologic		0.449		0.392		0.405
LGPUC vs HGPUC	0.5 (0.1-2.4)	0.410	2.2 (0.2-22.6)	0.503	0.6 (0.1-2.6)	0.501
LGPUC vs Mixt, Other	0.3 (0.1-1.9)	0.214	0.8 (0.1-10.1)	0.831	0.3 (0.1-1.9)	0.218
T Stage		0.641		0.304		0.643
T2 vs T1	1.6 (0.2-13.5)	0.652	0.9 (0.4-1.2)	0.986	0.8 (0.1-6.5)	0.849
T2 vs T3-4	1.5 (0.6-3.9)	0.383	2.5 (0.8-8.1)	0.123	1.5 (0.6-3.5)	0.372
Node Status						
N0 vs N1-2	0.6 (0.1-2.8)	0.507	0.9 (0.2-4.6)	0.899	0.7 (0.2-3.3)	0.676
Urothelial obstruction						
No vs Yes	3.6 (1.4-9.3)	0.007	5.6 (1.8-17.3)	0.003	2.7 (1.1-6.5)	0.031

Abbreviations: CI=confidence interval; HGPUC=high-grade papillary urothelial carcinoma; LGPUC= low-grade papillary urothelial carcinoma.

rate was 69.6% for patients with complete responses but dropped to 35.4% for patients with incomplete responses (P = 0.001). CSS was significantly better among the 76 patients who did not have urothelial obstruction at presentation. The two-year CSS rate was 93.3% for patients without urothelial obstruction at presentation but dropped to 68.4% for patients with urothelial obstruction ($p \leq 0.001$).

Toxicity

Grade 1 and 2 toxicities could not be evaluated due to the missing files and records of the patients. We recorded higher grade toxicities from registered nurses orders and patient recipes. Concurrent chemotherapy was interrupted in an overall four patients due to grade 3 hematological toxicities were observed. The percentages of patients sustaining acute bladder irradiation, fatigue, and diarrhea were 32%, 43%, and 10%, respectively. There were no late grade 4 toxicities and deaths attributable to the treatment.

DISCUSSION

Population aging is a shift in the distribution of people toward older ages with increasing life expectancy. Although age is known as a poor prognostic factor, the geriatric patient population is a heterogeneous group, and the chronological age of the patient does not always reflect their actual health status (8). To choose treatments wisely, an estimate

Table 4. Results of log-rank univariate analysis for disease-free survival

Variable	n	Median Survival (95% CI)	2-y DFS (%)	5-y DFS (%)	p value
Age (year)					
<70	23	14.9 (4.4-25.3)	40.9	40.9	0.825
70≤	70	28 (18-38)	53.2	25.2	
Gender					
Male	84	25.5 (14.9-36.2)	50.7	28.7	0.679
Female	9	17.9 (7.5-28.3)	50	25	
Tumor diameter (cm)					
≤5	46	32.3 (8.9-55.8)	53.4	35.2	0.686
>5	18	40.4 (0-86.7)	57.1	34.8	
Tumor histologic					
LGPUC	6	14.9 (0-54)	50	33.3	0.170
HGPUC	72	21.9 (13.5-30.2)	46.7	20.9	
Mixt, Other	15	67.2 (0-134.9)	69.2	52.7	
Histologic grade					
G1-G2	6	14.9 (0-54)	50	33.3	0.505
G3-G4	87	24.5 (14.9-34.2)	50.7	28	
T Stage					
T1	4	17.9 (6.8-29.1)	33.3	33.3	0.979
T2	70	25.5 (14-37.1)	50.5	27.8	
T3-4	19	24.5 (0-52)	53.5	28.5	
Node Status					
N0	80	25.5 (14.5-36.6)	51.5	28.2	0.906
N1-2	9	29.6 (19.8-39.4)	55.6	27.8	
Urothelial obstruction					
No	76	31.8 (13.4-50.2)	54.3	33.1	0.038
Yes	16	19.1 (7.1-31.2)	36.5	0	
Procedure					
Complete TUR	29	65 (25.1-105)	71.9	50.7	0.047
Incomplete TUR	62	21.1 (14.8-27.5)	43.3	20.9	
Treatment response					
No	25	43.5 (21.5-65.6)	21.2	6.4	<0.001
Yes	60	10.7 (6.5-15)	63.2	39	

Abbreviations: TUR=transurethral resection of the bladder, HGPUC= high-grade papillary urothelial carcinoma, LGPUC= low-grade papillary urothelial carcinoma; Mixt = adenosquamos;
Other = Squamos, adeno cancer, undifferentiated carcinoma, small cell carcinoma.

of life expectancy should be considered against the risk of cancer relapse or cancer-related death during treatment plan.

BC is an age-associated malignancy with increased prevalence in patients aged ≥ 65 years (9). Bladder tumors are the fourth most frequently diagnosed cancer type in males and the ninth in females (10). The histological grade of BC is eventually determined by examining the resected tumor. The most widely used classification for grading non-MIBC (G1, G2, and G3) was the 1973 World Health Organization (WHO) classification (11). However, a revised grading system for urothelial carcinoma (low grade and high grade) was proposed and adopted by the WHO in 2004 to replace the 1973 classification system. The natural history of BC is heteroge-

neous, ranging from a low-grade variant to a high-grade subtype (12,13). Wakai et al. reported the distribution of tumor grades were as follows: 74% high grade and 26% low grade (14). In our study high, low, and mixed grades were present in 77%, 7%, and 16% of patients, respectively.

Thus far, bladder-sparing approaches using RT alone have not yielded comparable results with radical cystectomy and lymphadenectomy. To improve the efficacy of radical RT, neoadjuvant or concomitant chemotherapy has been administered. Currently, platinum-based chemotherapy has been advocated for CRT as an alternative to radical cystectomy in MIBC (15). The most comprehensive TUR for invasive BC, followed by RT with the concurrent administration of cisplatin, was fairly well tolerated by the patients we studied. Treatment-related toxicities are generally reversible and comparable and are slightly lower than with other studies (16). The typical dose schedules of RT would be 64 Gy in 32 fractions or hypofractionated schedules such as 55 Gy in 20 fractions. Many studies have used 64–66 Gy, but the definite optimal RT dose is unknown (17). Korpics et al. conducted a retrospective cohort study involving 843 patients with cT2-4 N0-3 M0 transitional cell MIBC treated with RT and found that patients receiving RT were more likely to receive an RT dose of 60 Gy. The two-year OS rates, when divided by RT doses, were 26%, 31%, 56%, and 55% for <50, 50–59, 60–66, and >66 Gy, respectively, and analyses showed that <50 Gy doses were associated with worse survival outcomes (18). In our study, we utilized 64 Gy, and the two-year OS rate was 70.6%. The obtained OS rate was higher than that in Korpics et al.'s study, and this difference could be due to the addition of chemotherapy and RT technique.

Neoadjuvant or concomitant chemotherapy has been added to improve the efficacy of radical RT. The addition of chemotherapy is aimed to eliminate the micrometastases and increase the radiation sensitivity. In this way, the Radiation Oncology Group (RTOG) designed a series of studies that examined the efficacy of peritreatment chemotherapy. In the first study, RTOG 8512, 64 Gy RT with cisplatin was administered in 42 patients. The five-year OS rate with radiosensitizing cisplatin was 52% (19). The RTOG 99-06 study assessed the effect of chemotherapeutic agents on the weekly use of cisplatin and paclitaxel simultaneously with RT, and the five-year OS rate was reported to be 50% (20). The five-year survival reported by other authors ranged from 47% to 54%. Concurrent chemotherapy was continued in 80.7 % of patients. Gemcitabine was interrupted due to grade 3 thrombocytopenia in one patient (21). In our study, we found a five-year OS rate of 36.9 %, which is lower than those of other studies. This result may be due to the inclusion of more patients undergoing incomplete TUR and our cohort being older. Concurrent chemotherapy was given as a part of CRT in 89 patients (95. 6%).

There are two randomized trials of radiosensitization using UK schedules: the BC2001 and BCON studies. These trials use radiosensitization with either concurrent chemotherapy (BC2001) or carbogen and nicotinamide (BCON). BC2001 has shown significant improvement in DFS with concurrent 5-fluorouracil and mitomycin C of 34% (22,23). Hussain et al. reported a phase I/II study of synchronous CRT with mitomycin C and 5-FU in 41 patients and obtained two- and five-year OS rates of 49% and 36%, respectively (24). In our study, we found the two-year OS rates were 70.6% respectively, which is higher than those of the above-mentioned trials due to the addition of cisplatin.

The radicality of TUR in bladder-sparing treatment was reported to be an independent prognostic factor for the survival of patients with MIBC. Asadauskienė et al. showed a statistically significant difference between complete and incomplete TUR in terms of OS. Data from this study demonstrated an impact of patient age, T stage, and dose of radiation on survival of patients treated by radiotherapy. (25). In the current study, we characterized urothelial

Table 5. Results of log-rank univariate analysis for cause-specific survival

Variable	n	Median Survival (95% CI)	2-y CSS (%)	5-y CSS (%)	P value
Age (year)					
<70	23	63.9 (46.9-80.8)	84.6	65.8	0.731
70≤	70	65.9 (55.7-76)	89.9	57.4	
Gender					
Male	84	81.5 (65-98.1)	89.6	63.6	0.256
Female	9	25.4 (0-61.2)	83.3	33.3	
Tumor diameter (cm)					
≤5	46	69.3 (53.3-85.3)	88.6	66.2	0.357
>5	18	40.4 (13.1-67.6)	85.7	36.7	
Tumor histologic					
LGPUC	6	77.3 (64.3-90.2)	100	75	0.245
HGPUC	72	61.1 (50.4-71.7)	86	52.8	
Mixt, Other	15	79.3 (60.8-97.8)	100	80	
Histologic grade					
G1-G2	6	77.3 (64.3-90.2)	100	75	0.360
G3-G4	87	65.8 (56.2-75.4)	88.4	59.4	
T Stage					
T1	4	80.1 (63.2-97)	100	100	0.204
T2	70	70.8 (60.7-81)	89.1	68.7	
T3-4	19	51.6 (34.5-68.7)	87.1	31.7	
Node Status					
N0	80	81.5 (59.5-103.5)	90.4	60	0.339
N1-2	9	34.3 (4.6-64)	76.2	38.1	
Urothelial obstruction					
No	76	97 (65-128.9)	93.3	67.9	<0.001
Yes	16	33.5 (13.8-53.3)	68.4	0	
Procedure					
Complete TUR	29	73.9 (57.4-90.3)	91.1	62.3)	0.371
Incomplete TUR	62	63.7 (52.4-75)	87.7	58	
Treatment response					
No	25	48.1 (27.8-68.4)	75.1	35.4	0.001
Yes	60	74.9 (64.9-84.9)	94	69.6	

Abbreviations: TUR=transurethral resection of the bladder, HGPUC=high-grade papillary urothelial carcinoma, LGPUC= low-grade papillary urothelial carcinoma

obstruction and the status of treatment response as significant prognostic factors that predict OS and CSS in the univariate analysis. However, the status of treatment response lost its statistical significance when included in a multivariate analysis with the factors that were significantly associated with survival in the univariate analysis. Considering the likelihood of 76 patients without urothelial obstruction surviving two years with a functioning, treated bladder (54.3%), the bladder-sparing approach is relatively encouraging compared to 16 (36.5%) patients with urothelial obstruction.

Study Limitations

Our study includes the following limitations: first, our study was single institutional and retrospective; and second, T stage was not detected as a significant prognostic factor for a relatively small number of patients.

CONCLUSION

Our study supports the utilization of CRT for BC in routine practice. Concomitant cisplatin was administered in all patients without any omission due to toxicity. There was no grade 3 intestinal or genitourinary side effects recorded. Grade 3 hematologic post-treatment toxicity occurred in four patients.

The authors declare no conflict of interest.

Funding: The funders had no role in the study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

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