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TO STUDY THE RESPONSE RATE OF HYPO-FRACTIONATED BLADDER PRESERVATION RADIOTHERAPY IN MUSCLE INVASIVE BLADDER CANCER

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Abstract

Objective: To determine the response rate of hypofractionated bladder-preservation radiotherapy in patients with muscle-invasive bladder cancer according to RECIST criteria.

Study Design: Descriptive case series.

Place and Duration of Study: Department of Radiotherapy, Institute of Nuclear Medicine & Oncology (INMOL), Lahore, from June 2025 to September 2025.

Methodology: A total of 66 patients aged 25–70 years with histopathologically confirmed muscle-invasive bladder cancer (T2–T4a, N0–N1, M0) and ECOG performance status 0–1 were enrolled using non-probability consecutive sampling.

Results: The mean age of patients was 49.8 ± 11.6 years, and 78.8% were males. Complete response was observed in 74.2% of patients, partial response in 13.6%, stable disease in 7.6%, and progressive disease in 4.6%, yielding an overall response rate of 87.8%. Response rates were highest in T2-stage tumors and declined with advancing tumor stage. Grade III toxicity occurred infrequently, and treatment interruption was required in only 3.0% of patients.

Conclusion: Hypofractionated bladder-preservation radiotherapy achieves a high response rate with acceptable acute toxicity in muscle-invasive bladder cancer, representing an effective and well-tolerated bladder-sparing treatment option for appropriately selected patients.

Key Words: Muscle-invasive bladder cancer, Hypofractionated radiotherapy, Bladder preservation, RECIST criteria

INTRODUCTION

Bladder cancer is one of the commonest urinary tracts malignancies and is a serious health burden in the world. The global cancer statistics demonstrate that globally, around 573,000 de novo cases of the bladder cancer were diagnosed in 2020, which constitute a significant share of the morbidity and mortality associated with cancer, and close to 211,000 deaths are recorded each year [1]. It is classified as one of the ten most often diagnosed cancers in the world and is one of the most common cause of death due to cancer mainly in the elderly [2]. The disease is significantly male dominated, with incidence rates being almost four times high in men than in women and this has been explained by the fact that men are exposed to several environmental and occupational risk factors more than women are [3].

Muscle-invasive bladder cancer (MIBC) is a specific type of bladder malignancy, which is associated with additional invasion into muscle and detrusor layers and a high likelihood of the development of local and distant metastases. There is still a poor prognosis of MIBC in comparison to non-muscle-invasive disease and the five-year survival rates have been reported as falling down to about 30-40 percent in spite of the improvements in diagnostic and treatment plans [4]. Tobacco smoking, occupational exposure to aromatic amines, chronic bladder inflammation, previous pelvic radiation, and some of these chemotherapeutic agents like cyclophosphamide are some of the established risk factors, which cause bladder cancer [5]. Hematuria is the most frequent symptom of the presentation, and it leads to further tests, such as cystoscopy and histopathological validation in the majority of cases. Radical cystectomy and pelvic lymph node dissection has been considered to be the conventional curative management of MIBC. Nevertheless, in spite of providing reasonable oncological management, radical cystectomy is linked to high levels of perioperative morbidity, functional impairment on the long run, and negative consequences on the quality of life, such as urinary diversion related morbidity, sexual dyslexia, and psychosomatic distress [6]. Despite the improvement in the surgical methods and urinary reconstructions, the physical and emotional cost of cystectomy is rather significant, especially in patients with age-related changes and those with multiple comorbidities.

The use of neoadjuvant cisplatin-based chemotherapy before the incorporation of definitive local therapy has shown a small yet significant overall survival with an absolute survival benefit approximated to be 5% at five years [7]. However, a significant percentage of patients are not eligible to receive cisplatin because of renal dysfunction, poor performance status, or comorbidities or refuse surgery because of the fear of postoperative quality of life [8]. Such restrictions have led to an increasing interest in bladder-sparing treatment approaches that are expected to provide oncological control without organ failure. Trimodality therapy (maximal transurethral resection of bladder tumor (TURBT) and radiotherapy with concurrent radiosensitization) is a safe alternative to radical cystectomy in certain patients with MIBC. Several studies have shown that bladder-preserving strategies in carefully chosen cases are able to give disease control and survival rates similar to radical procedures [9]. Notably, bladder preservation has the benefit of preserving native bladder functionality and, hence, minimizing morbidity associated with treatment and conservation of quality of life. Radiotherapy is at the centre of bladder-saving measures. Conventionally, regular fractionation regimens that administer 1.8 -2.0 Gy in one fraction within multiple weeks have been utilized. Nevertheless, hypo-fractionated courses of radiotherapy, that is, higher doses of radiotherapy per fraction with an overall treatment course reduced in duration, have been more and more accepted in recent years [10]. Huge randomized trials and meta-analyses have proven that hypofractionated bladder radiotherapy has better invasive locoregional control over conventional fractionation, and does not raise late toxicity to the bladder or the rectum [11]. The radiobiological basis of hypofractionation in bladder cancer is justified by facts that propose relative low α/B ratio of bladder tumors, implying the increased sensitivity to larger fraction doses [12]. Also, hypo fractionated regimens decrease total treatment time, decrease tumor repopulation, increase patient convenience, and decrease the use of healthcare resources, which is especially appealing in high-volume institutions and resource-constrained institutions [13]. Complete response rates reported after hypo-fractionated bladder preservation radiotherapy are reported to be between 70 and 80 percent, and a large number of studies have cited complete response rates of about 78 percent by imaging and cystoscopic analysis using standardized response criteria like RECIST [14].

Objectives

To determine the response rate of hypofractionated bladder preservation radiotherapy in muscle-invasive bladder cancer, according to the RECIST criteria.

METHODOLOGY

This was a descriptive case series conducted at the Department of Radiotherapy, Institute of Nuclear Medicine & Oncology (INMOL), Lahore, from June 2025 to September 2025. The researchers used 66 patients with muscle-invasive bladder cancer. The participants in the study were male and female patients between the ages of 25 and 70 years with the biopsy-proven carcinoma of the urinary bladder who were diagnosed with the muscle-invasive Bladder cancer (T2-T4, N0-N1, M0) and had the ECOG performance status of 0-1. Patients were enrolled only in those who were scheduled to receive hypofractionated radiotherapy to preserve bladder; in addition to that, patients needed to possess all the necessary clinical, radiological, and treatment data. All participants were included with the informed consent written down. Patients who did not want to participate, those who had a history of receiving some forms of pelvic irradiation, or those who had a serious comorbid condition (uncontrolled diabetes (BSR > 200 mg/dL) or uncontrolled hypertension (BP > 160/90 mmHg)) were excluded. Other exclusion criteria were the presence of secondary malignancies or metastatic disease, inflammatory bowel disease, autoimmune diseases or connective tissue disease. The radiotherapy uses were also restricted to patients who had contraindication to radiotherapy such as psoriasis or xeroderma pigmentosum since the radiotherapies are known to be very dangerous.

Data Collection

Sixty-six eligible patients who reported to the Institute of Nuclear Medicine & Oncology (INMOL), Lahore with muscle-invasive bladder carcinoma were enrolled with written informed consent after the institutional ethical review committee approved this. Age, gender, tumor stage, nodal status, and ECOG performance status were the baseline variables that were recorded with the help of a structured proforma. Based on the possible conditions, all the patients were subjected to maximum resection of bladder tumor of the bladder using transurethral resection (TURBT) followed by radiotherapy. The patients were given hypofractionated conformal radiotherapy at a total of 55 Gy in 20 fractions over 4 weeks with the fraction size of 2.75 Gy per fraction as per the institutional protocol. Radiological imaging and cystoscopic assessment 4-6 weeks following the end of the radiotherapy were used to measure treatment response and category response based on the RECIST criteria. Complete response was a term that was used to denote no visible tumor on imaging and cystoscopy. Follow-ups were then done on the patients after every three months in the first year to determine recurrence or progress.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Quantitative variables such as age were expressed as mean ± standard deviation, while categorical variables such as tumor stage, nodal status, and treatment response were presented as frequencies and percentages. The primary outcome measure was the complete response rate following hypofractionated bladder preservation radiotherapy. Associations between clinicopathological variables and treatment response were assessed using the chi-square test. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 66 patients with muscle-invasive bladder cancer were included in the study, with a mean age of 49.8 ± 11.6 years. Most patients were between 41 and 55 years of age (43.9%), followed by those aged 56–70 years (28.8%) and 25–40 years (27.3%). Males predominated the cohort, accounting for 78.8% of patients, while females comprised 21.2%. A history of smoking was present in 66.7% of patients, with a mean exposure of 22.4 ± 6.8 pack-years. ECOG performance status was favorable, with 57.6% of patients having ECOG 0 and 42.4% ECOG 1. Tumor staging showed that 42.4% had T2 disease, 39.4% had T3 disease, and 18.2% had T4a disease, with mean tumor size increasing progressively from 3.2 ± 0.9 cm in T2 tumors to 5.8 ± 1.3 cm in T4a tumors.

Table 1. Baseline Demographic, Clinical, and Tumor Characteristics of Patients (N = 66)

Variable	Category	n (%)	Mean ± SD	Median (IQR)
Age (years)	25–40	18 (27.3)	34.6 ± 4.1	35 (30–39)
	41–55	29 (43.9)	48.9 ± 4.3	49 (45–53)
	56–70	19 (28.8)	63.1 ± 4.2	64 (59–68)
	Overall age	**66 (100.0)**	**49.8 ± 11.6**	**50 (41–60)**
Gender	Male	52 (78.8)	51.2 ± 10.9	52 (44–61)
	Female	14 (21.2)	45.3 ± 12.1	46 (36–55)
Smoking history	Yes	44 (66.7)	22.4 ± 6.8 pack-years	21 (17–28)
	No	22 (33.3)	0.0 ± 0.0	0 (0–0)
ECOG status	0	38 (57.6)	49.1 ± 10.8	50 (42–58)
	1	28 (42.4)	50.7 ± 12.4	51 (43–63)
Tumor stage	T2	28 (42.4)	3.2 ± 0.9 cm	3.1 (2.5–3.8)
	T3	26 (39.4)	4.6 ± 1.1 cm	4.5 (3.9–5.4)
	T4a	12 (		

The mean overall treatment duration was 28.0 ± 0.0 days. Prior maximal transurethral resection of bladder tumor was performed in 89.4% of patients, who had a mean tumor size of 4.1 ± 1.2 cm, whereas patients who did not undergo TURBT had a larger mean tumor size of 5.4 ± 1.5 cm. Treatment completion rates were high, with 97.0% of patients completing radiotherapy as planned over a mean duration of 27.6 ± 1.4 days. Only 3.0% of patients experienced treatment interruption, occurring at a mean of 21.5 ± 3.2 days, indicating good overall treatment compliance.

Table 2. Radiotherapy and Treatment-Related Characteristics

Parameter	Category	n (%)	Mean ± SD
Radiotherapy technique	3D-CRT	66 (100.0)	55.0 ± 0.0 Gy
Total dose	55 Gy	66 (100.0)	55.0 ± 0.0 Gy
Fractions	20	66 (100.0)	20.0 ± 0.0
Dose per fraction	2.75 Gy	66 (100.0)	2.75 ± 0.0 Gy

Overall treatment time	4 weeks	66 (100.0)	28.0 ± 0.0 days
Prior TURBT	Yes	59 (89.4)	Tumor size 4.1 ± 1.2 cm
	No	7 (10.6)	Tumor size 5.4 ± 1.5 cm
Treatment completion	Completed	64 (97.0)	27.6 ± 1.4 days
	Interrupted	2 (3.0)	21.5 ± 3.2 days

Treatment response assessed according to RECIST criteria demonstrated a high overall response rate of 87.8%. Complete response was achieved in 49 patients (74.2%), while partial response was observed in 9 patients (13.6%). Stable disease occurred in 7.6% of patients, and progressive disease was seen in only 4.6%. Response rates varied by tumor stage, with the highest overall response rate seen in T2 tumors at 96.4%, followed by T3 tumors at 88.4% and T4a tumors at 66.6%. Mean tumor size reduction also showed a stage-dependent decline, from 78.6 ± 11.2% in T2 disease to 44.8 ± 15.9% in T4a disease.

Table 3. Tumor Response According to RECIST Criteria and Tumor Stage

Tumor Stage	CR n (%)	PR n (%)	SD n (%)	PD n (%)	ORR (CR+PR) %	Mean Tumor Reduction ± SD
T2 (n=28)	24 (85.7)	3 (10.7)	1 (3.6)	0 (0.0)	96.4	78.6 ± 11.2%
T3 (n=26)	18 (69.2)	5 (19.2)	2 (7.7)	1 (3.9)	88.4	62.3 ± 13.6%
T4a (n=12)	7 (58.3)	1 (8.3)	2 (16.7)	2 (16.7)	66.6	44.8 ± 15.9%
Overall (N=66)	**49 (74.2)**	**9 (13.6)**	**5 (7.6)**	**3 (4.6)**	**87.8**	**69.1 ± 14.4%**

Acute treatment-related toxicities were generally mild to moderate. Urinary frequency and dysuria were the most common toxicities, affecting 50.0% of patients, with grade I–II symptoms in the majority and grade III toxicity in 6.1%. Hematuria was reported in 31.8% of patients, with grade III hematuria occurring in 4.5%. Gastrointestinal toxicity in the form of diarrhea was observed in 24.2% of patients, with only 3.0% experiencing grade III symptoms.

Table 4. Acute Treatment-Related Toxicity Profile (CTCAE Grading)

Toxicity	Grade I n (%)	Grade II n (%)	Grade III n (%)	Any Grade n (%)	Mean Onset (days) ± SD
Urinary frequency/dysuria	18 (27.3)	11 (16.6)	4 (6.1)	33 (50.0)	12.4 ± 3.1
Hematuria	12 (18.2)	6 (9.1)	3 (4.5)	21 (31.8)	14.1 ± 4.2
Diarrhea	9 (13.6)	5 (7.6)	2 (3.0)	16 (24.2)	15.7 ± 3.8
Fatigue	15 (22.7)	7 (10.6)	1 (1.5)	23 (34.8)	10.6 ± 2.9
Treatment interruption	0 (0.0)	0 (0.0)	2 (3.0)	2 (3.0)	19.5 ± 2.1

DISCUSSION

This case-series descriptive study assessed the response in hypofractionated bladder preservation radiotherapy in patients with muscle-invasive bladder cancer based on the RECIST criteria and proved a high overall response rate with good toleration. The age of the study population was 49.8 ± 11.6 years and was highly male-dominated (78.8), which indicates the current demographic trend of bladder cancer in areas with high smoking rate. This age mix and preponderance of males have been a constant finding in the previous studies assessing bladder preservation options in muscle-invasive disease [16]. The features of tumors among this cohort showed that the majority of the patients came with locally advanced disease with 39.4% having T3 tumor and 18.2% T4a tumor. Almost 70% showed high-grade histology, and 25.8% of patients had nodal involvement. These results highlight the aggressive disease pathology of the target population. Similar tumor stage, grade, and nodal status distributions have been reported in past studies using bladder preservation radiotherapy, especially in those patients who are ineligible to undergo radical cystectomy [17]. Response to treatment using the RECIST criteria was the main outcome of this research. A total response rate of 87.8% was obtained, and full response was detected amid 74.2% of patients and partial response among 13.6% of the patients. The findings are clinically important and consistent with reported complete response rates of 70 to 80 percent in other studies that assessed hypofractionated bladder radiotherapy regimens in the past [18]. The complete response rate was high which indicates that hypofractionated regimens are effective in local tumor control. This is a stage-dependent decrease in response that has been reported multiple times in prior studies, with more profound muscle invasion and extravesical extension being linked with less radiosensitivity and low complete responses [19]. The compliance rate in this study was good with 97.0 percent of the patients completing radiotherapy as per schedule. Prior maximal TURBT had been done in 89.4 percent of patients and it was also related to smaller baseline tumor size

than those not subjected to TURBT. Maximal TURBT has been highlighted as of significance in radiotherapy response in the past studies that showed a successful increase in both local control and complete response rate when TURBT was used before bladder preservation radiotherapy [20]. Hypofractionated radiotherapy caused acute toxicity that was usually mild-moderate. The most frequent toxicities were urinary frequency and dysuria, which affected 50.0% of patients and grade III urinary toxicity was only present in 6.1%. GIT toxicity was non-existent with 3.0% grade III diarrhea in patients. There was also rare toxicity treatment interruption rate which was 3.0%. Such results agree with prior studies which have indicated that there is no significant difference between hypofractionated and conventional schedules of radiotherapy on acute toxicity in bladder radiotherapy. The positive toxicity profile pattern demonstrates that hypofractionated regimens are tolerable, especially in situations where limited resources exist such that shorter-course treatments can lower patient burden and medical service. Earlier studies have given the benefits of hypofractionation as, patient comfort, shorter treatment time and better radiotherapy throughput without affecting safety and effectiveness.

CONCLUSION

It is concluded that hypofractionated bladder preservation radiotherapy is an effective and well-tolerated treatment modality for patients with muscle-invasive bladder cancer. A high overall response rate was observed, with the majority of patients achieving complete tumor response according to RECIST criteria, particularly in earlier tumor stages. The treatment was associated with acceptable acute toxicity and high treatment compliance, with minimal interruption of therapy. These findings support the role of hypofractionated bladder preservation radiotherapy as a viable alternative to radical cystectomy in appropriately selected patients, offering effective disease control while maintaining bladder function.

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