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Pelvic Nodal Irradiation in Muscle Invasive Bladder Cancer (MIBC)

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Abstract

Background: Bladder cancer preservation treatment achieved 5/10-year overall survival rates comparable to those of radical cystectomy. Bladder-preserving trials have recommended coverage of pelvic lymph nodes (LN) in radiation portals (micrometastases in pelvic LN 25 to 44%). Gemcitabine-based radiotherapy did not include the pelvic LN in the radiation portals to minimize bowel toxicity. However, the pelvic LN irradiation debate has been highlighted. The present study aimed to evaluate the role of pelvic LN irradiation in negative node, bladder cancer.

Method: A prospective study was conducted from October 2017 to February 2020 at the South Egypt Cancer Institute. Bladder cancer Patients with cT1-3, N0, and M0 underwent maximum TURBT and were then randomized into two arms: Group A: Bladder-only irradiation (52.5 GY/20 frs); Group B: Pelvic nodal irradiation with weekly gemcitabine 100mg/m2

Statistical analysis: SPSS Statistics (version 26.0, IBM), descriptive (means and SD), chi-square test for qualitative variables, independent student t-test, and survival analysis (Kaplan-Meier).

Results: Patients aged 37 to 76 years old and 32 to 82 years old in groups A and B, respectively. Cases were Stage III in groups A, II, and III in B. Both groups showed similar local control rates (90% and 92%, respectively). Favorable toxicity profile group A schedule emphasizes high local control with low-grade intestinal toxicity (no G3 enteritis). Unexpectedly, Group A showed significantly higher progression free survival (PFS) over Group B ($P < 0.034$).

Conclusion: Bladder-only chemoradiation has non-inferior local control of node-negative bladder cancer with significantly higher PFS. The pelvic nodal radiation field has an unfavorable toxicity profile (higher G2 enteritis).

Keywords: Pelvic radiation, Radiotherapy, Urologic neoplasms, Muscle invasive carcinoma, Hypofractination

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Introduction

Bladder cancer is the most common malignancy involving the urinary system and the tenth most common malignancy globally.[1] An estimated 83,190 new cases of urinary bladder cancer (63,070 males and 20,120 females) expected to be diagnosed in the United States in 2024 with approximately 16,840 deaths (12,290 males and 4550 females) during this same period Bladder cancer, the sixth most common cancer in the United States, is rarely diagnosed in individuals <40 years.[2]

Urothelial carcinoma in bladder represents the 10th type of cancer worldwide, as 549,000 new cases per year. The highest incidence rates in Europe are observed in Southern Europe. For instance, Greece (5800 new cases and 1537 deaths in 2018), Spain and Italy, and in Western Europe, Belgium and the Netherlands. The most important risk factor for developing bladder cancer is tobacco smoking, which accounts for 50% of cases, followed by occupational exposure to aromatic amines and ionizing radiation. European Society of Medical Oncology (ESMO) guidelines 2014 updated reports in Europe, 151,297 new cases of bladder cancer were diagnosed in 2012, with an age-standardized incidence rate (per 100,000 persons) of 17.7 for males and 3.5 for females. Overall, the annual crude incidence rate is 20.4/100,000. In 2012, there were 52 395 deaths from bladder cancer with an annual crude mortality rate of 7.1/100,000. Approximately 70% of patients with bladder cancer are >65 years of age.[3]

Muscle invasive bladder cancer (MIBC) is considered curable as achieved with radical cystectomy or radiation therapy (RT) alone or radio-chemotherapy (RCT). Chemotherapy (CT) contributions may be administered as neoadjuvant or concurrent. Although no randomized studies of RT/RCT vs surgery, reports showed comparable rates of 5 years cause-specific survival: approximately 50%. The implementation of treatment protocols involving transurethral resection of urinary bladder tumors (TURBT) or radiotherapy (RT), even when applied in varying sequences alongside chemotherapy (CT), has demonstrated the capacity to yield overall survival (OS) rates at the 5- and 10-year mark that are comparable to those achieved through radical cystectomy. Recent updates indicate that the 5-year survival rates range from 50% to 67%, with approximately 75% of patients who survive managing to retain their own bladder. Achieving complete response (CR) is seen in >70% of patients with MIBC.

Old cystectomy series in bladder cancer showed 40% risk of micrometastases of pelvic lymph nodes (PLNs). The survival impact by treatment modalities that use exclusive bladder radiation versus those that include both bladder and PLN radiation remains unclear and serves as the primary focus of this investigation.[4]

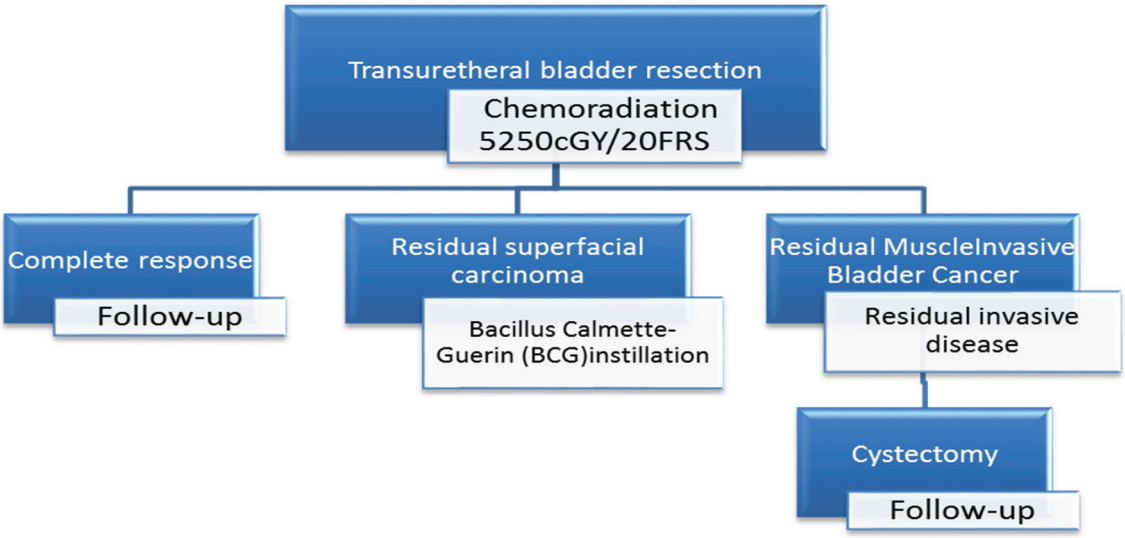
By contrast, trials incorporating newer CT agents (gemcitabine, paclitaxel) with radiation did not include the pelvic LN in the radiation portals to minimize the bowel toxicity. There is, however, an ongoing debate whether or not pelvic LN irradiation should be done and the role of pelvic LN irradiation in patients with LN negative muscle-invasive bladder cancer has not yet been examined in detail, to our knowledge.

Therefore, the present study aimed to answer the question of the beneficial role of pelvic LN irradiation for patients with LN_ muscle-invasive bladder and whether pelvic LN irradiation can be omitted if is not beneficial.

Material and Methods

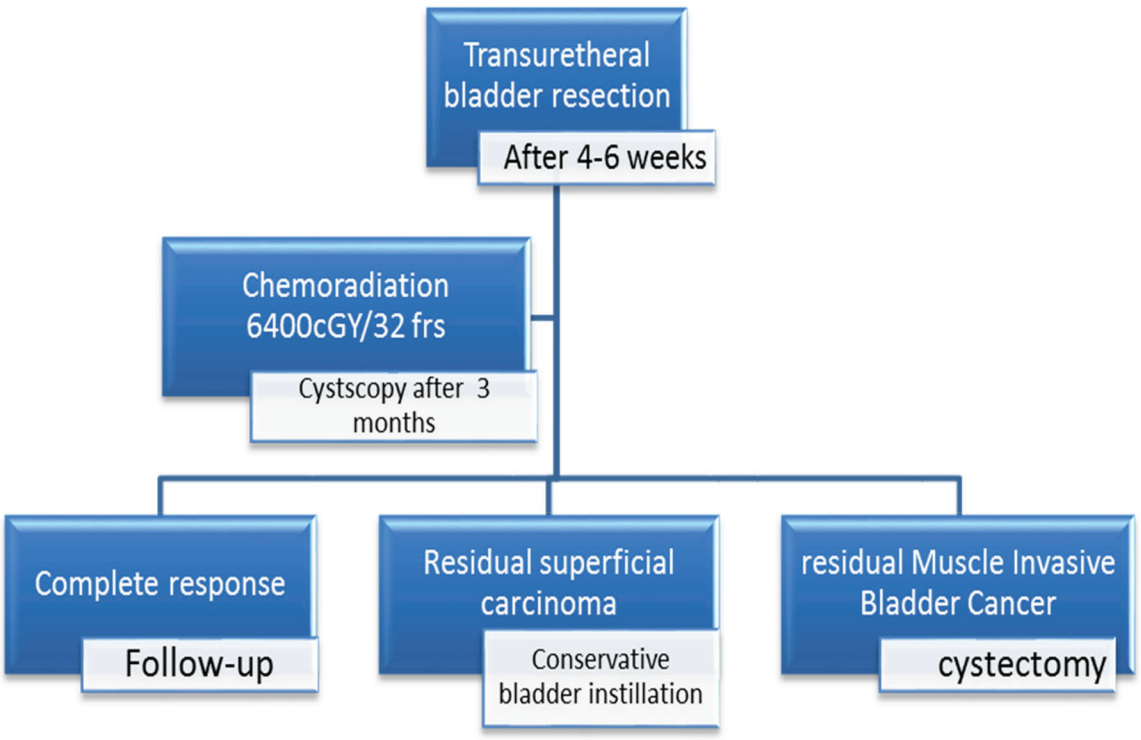
Between October 2017 and February 2020, 51 patients with histologically confirmed muscle-invasive bladder cancer were accrued and were treated for bladder preservation. The study protocol was approved by South Egypt Cancer institutional ethical committee (ethics code: SECI IRB./IORG0006563). All patients gave written consent for treatment.

This prospective study was conducted during the period from October 2017 to February 2020 in the radiotherapy department, South Egypt Cancer Institute, clinical oncology department and urology hospital, faculty of medicine, Assiut University. Informed consent was obtained from all recruited patients with Institutional Review



Algorithm 1. Treatment protocol received by patients in group A, Bladder only radiation

Board approval for the protocol. Patients with cT1-3, N0, M0 bladder cancer who underwent maximum TURBT were eligible for the study. Pretreatment evaluation of patients included chest radiograph, abdomen-pelvic magnetic resonance imaging (MRI)/ bone scan (if ≥T3, bone pain or elevated alkaline phosphatase), complete blood count, renal and hepatic function tests, ECOG scoring performance status ≤ 2, hemoglobin ≥ 10 mg/dl, an absolute neutrophil ≥1500/ml, a platelet count of > 100,000/mm3, a serum creatinine of ≤1.5 mg, a serum bilirubin ≤ 1.3 time. Patients with previous pelvic RT patients with node positive disease or evidence of distant metastasis (M1) were excluded from study. All patients in this study underwent maximum



Algorithm 2. Treatment protocol for patients in Group B (whole pelvic radiation)

transurethral resection of bladder cancer. Treatment was started within 4-6 weeks after the maximal transurethral resection by randomizing patients into two arms:

Group A Bladder Only Irradiation: patients received chemo radiation course. Aiming to deliver 52.50 GY/20 fractions to tumor and bladder. The chemotherapy agents included gemcitabine 100 mg/m2 given as a 30-minute intravenous infusion 2 to 4 hours before RT. Gemcitabine was administered once per week during RT on days 1, 8, 15, and weekly as radiation sensitizer (Algorithm 1).

• Group B pelvic nodal irradiation: Patients received chemoradiation course that delivered 64GY/32fractions with the same dose of Gemcitabine (Algorithm 2).

Radiotherapy planning

All patients were planned through Computerized tomography simulator-based planning with isocentric technique.

In group A: regarding Clinical target volume, CTV, covering the bladder with circumferiential 1.5 cm margins. Based on low relapse incidence of lymph node in old studies and as per the ASCO recommendations. Planned target volume (PTV) had included CTV+1 cm to account for set up uncertainties. Conformal technique was used to conform distribution of isodose line (95% covering the (PTV), not exceeding tolerance of rectum.

Clinical target volume (CTV) had included the whole bladder + 1.5 cm margins all around and excludes rectum and small intestine). In this group, patients received hypo-fractionated radiation schedule in form of 5250cGy/20 fractions by 262.5cGyper fraction, over 4 weeks with weekly gemcitabine 100 mg/m2, as shown in Figure 1.

In-group B: Two phases technique. In phase one, PTV had to cover the bladder, lymphatic plus 2 cm margins to account for setup errors. A three-field technique (anterior and 2 lateral) was used so that the posterior border of lateral fields has included anterior rectum (not reach maximum tolerance of rectum) with line pass through S2-S3 inters pace. The superior border was located at a horizontal line drawn through the interspace between L5-S1 and lateral borders 1.5 cm of pelvic prim. The inferior border of all fields was located below the lower margin of obturator

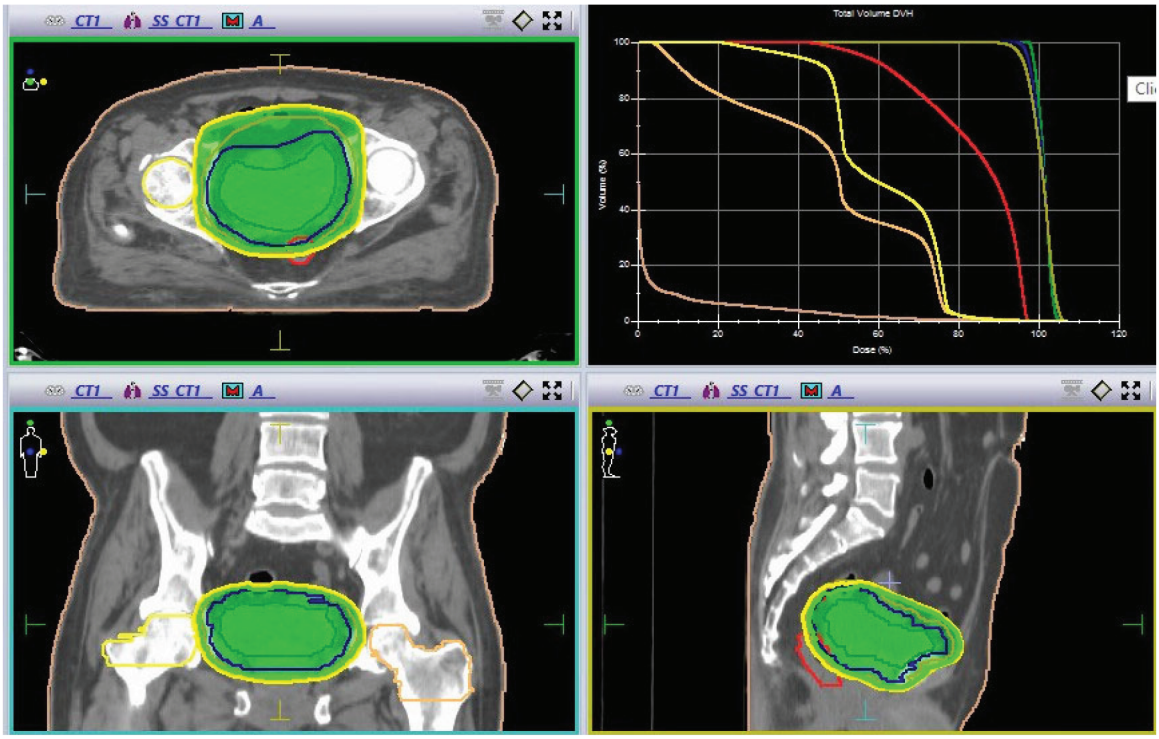


Figure 1. This figure shows the bladder only plan for T3N0M0 bladder cancer, patient with 3D conformal Radiotherapy technique, (Inner to be in radiotherapy technique Quaderant Ratio) dose to the bladder was 53.93 Gy.

Table 1. Patient's Demographics in groups A (bladder only radiation) and B (whole pelvic radiatiSon)

Variable	Group A N = 33		Group B N = 18		Total N = 51 N (%)	*P*-value
	N	%	N	%		
Age@						
Mean ± SD	59.42 ± 9.63		61.78 ± 11.21			0.435
Range	37-76		32-82			
Sex ^						
Male	32	97%	16	88.9%	48 (94.1%)	0.282
Female 1	3%	2	11.1%	3 (5.9%)		
Performance^						
I	1	3%	-	-	1 (2%)	0.710 (NA)
II	21	63.7%	10	55.6%	31 (60.8%)	
III	11	33.3%	8	44.4%	19 (37.2%)	
Hypertension^						
Yes	4	12.1%	2	11.1%	6 (11.8%)	1.000
No	29	87.9%	16	88.9%	45 (88.2%)	
Piles^						
Yes	7	21.2%	4	22.2%	11 (21.6%)	1.000
No	26	78.8%	14	77.8%	40 (78.4%)	
Smoking^^						
Yes	22	66.7%	11	61.1%	33 (64.7%)	0.692
No	11	33.3%	7	38.9%	18 (35.3%)	
Bilharziasis^						
Yes	27	81.8%	16	88.9%	43 (84.3%)	0.696
No	6	18.2%	2	11.1%	8 (15.7%)	

@ Independent sample student t-test was used; ^ Fisher's Exact test was used; ^^ Chi-square test was used; N: Number

foramen. Conventional radiotherapy schedule of 44Gy/22 frs upon 200cGy per fraction/over 4.5 weeks and patients received weekly gemcitabine 100mg/m2.

In phase two, CTV had included the bladder +1.5 cm margins all around. PTV had included CTV+1 cm margins. Patients received conventional radiotherapy schedule 20Gy /10 frs prescribing 2Gy per fraction/ 2 weeks and receiving weekly gemcitabine 100mg/m2.

Evaluation of treatment

Acute treatment related toxicity was assessed weekly during treatment and on the final day of treatment. After completion of treatment, acute toxicity was scored for additional 6 weeks and expressed using the RTOG/EORTC Radiation Toxicity Grading.

Late treatment related toxicity was assessed monthly up to one year starting from 6 weeks from end of chemoradiation course and then every 6 months with time of cystoscopy and imaging evaluation. Patients were assessed based on RTOG/EORTC Radiation Toxicity Grading.

Treatment interruption

If any grade 3 hematological toxicity develops, chemoradiotherapy should be discontinued for one week. For a grade 3 in field (radiation-related) toxicity during any treatment week (such as radiation cystitis, acute colitis), chemotherapy and radiation therapy should be delayed until resolution of toxicity to grade 2 or less. If there was any gap period, patient had to resume but if ≥three weeks, the patient should be considered intolerant to protocol therapy and considered off-protocol and will be referred to radical cystectomy.

Assessment of response to treatment

Response to treatment was evaluated 3 months after completion of treatment by MRI scans of the abdomen and pelvis together with cystoscopy under general anesthesia with biopsy from any suspicious lesion. Additional cystoscopy was performed at 7 and 12 months and every 6 months thereafter. Repeat MRI scans were undertaken at 12 months and 24 months. CR was defined as the absence of visible tumor endoscopically and the absence of histologic evidence of disease.

Statistical analysis

OS was defined as the time from diagnosis

till death or last follow-up visit at time of analysis.

Progression-free survival (PFS) was defined as the time from diagnosis till time of clinical, radiological progression OR death.

- Data entry and cleaning were done using Excel program. Then, the data were converted to SPSS Statistics (version 26.0, IBM) to be analyzed.
- The analysis included descriptive statistics (in the form of frequencies, percentages, means and SD).
- Chi-square test (x2 test) and Fisher Exact test were used to compare between qualitative variables.
- Independent sample student t-test was used to compare between two sample means.
- Survival analysis was determined using Kaplan Meier method. Log–rank test was used to compare between survivals of two treatment groups.

P-value was considered significant when it was equal or less than 0.05.

Results

This prospective randomized study included 51 eligible patients with bladder cancer. Patients were assigned to two different radiation schedules, 33 patients in group A and 18 patients in group B.

Patients' characteristics

The age distribution of patients ranged between 37 to 76 years old in group A and 32 to 82 years old in group B. Males presented 97% in group A and 89% in group B while females presented 3% in group A and 11% in group B (Table 1).

In our study, all bladder Cancer patients underwent maximum transurethral resection of bladder cancer. Treatment was started within 4-6 weeks after the maximal transurethral resection before randomization. With staging work up according to standard investigation and AJCC, most of cases were Stage III in group A but II and III in group B. Thus, there was no significant difference between groups regarding stage grouping, as shown in Table 2.

Most of patients in group B were regular in treatment but 10 patients (19%) were in irregular cycles of chemotherapy.

After assessment of treatment in both groups, 81.8% of Group A achieved CR. However, 67% in Group B, which is great impact of local control in both groups with non-inferiority of bladder, achieved only radiation (Table 3).

Patients in both study groups showed similar local control rate (92.6% and 92%, respectively). In group A, two patients experienced local recurrence (T3 and G3) but those in group B,

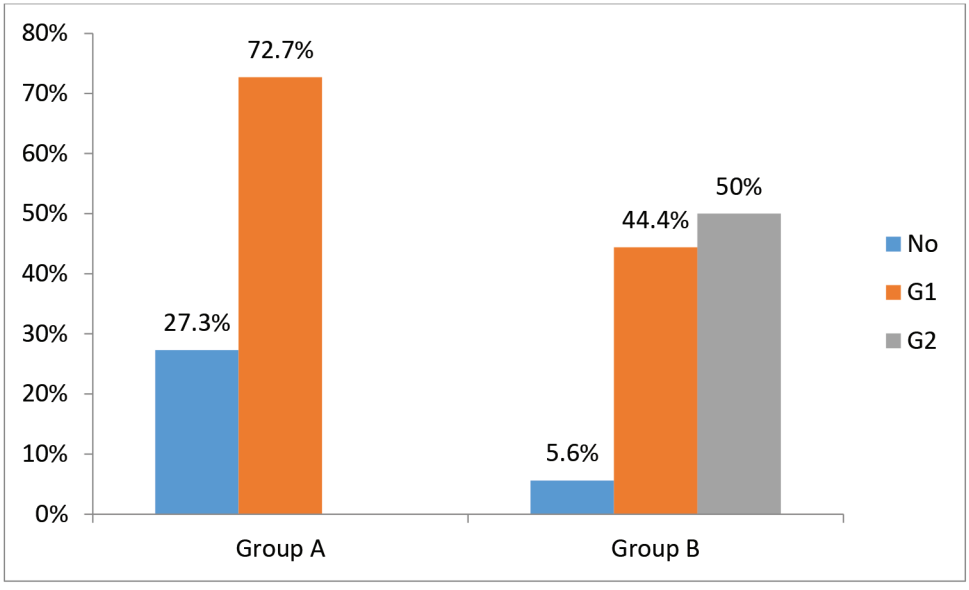


Figure 2. This figure shows the intestinal toxicity profile among the patients with bladder cancer in both study groups A (bladder only radiation) and B (whole pelvic radiation)

Table 2. Descriptive analysis of both study groups A (bladder only radiation) and B (whole pelvic radiation) showed no significant difference regarding tumor stage and pathological features

Variable	Group A N = 33		Group B N = 18		Total N = 51 N (%)	*P*-value
	N	%	N	%		
Grade^						
Poorly-differentiated	25	75.8%	13	72.2%	38 (74.5%)	1.000
Moderate- and well-differentiated	8	24.2%	5	27.8%	13 (25.5%)	
Stage^^						
I	1	3%	2	11.1%	3 (5.9%)	0.073
II	15	45.5%	12	66.7%	27 (52.9%)	
III	17	51.5%	4	22.2%	21 (41.2%)	
Chemotherapy^						
Regular	23	69.7%	18	100%	41 (80.4%)	0.009*
Irregular	10	30.3%	-	-	10 (19.6%)	

^Fisher's Exact test was used; ^^Chi-square test was used; **P*-value <0.05 was significant; N: Number

Table 3. Comparable treatment response between both study groups A (bladder only radiation) and B (whole pelvic radiation)

Response at the end of ttt^	Group A	%	Group B	%	Total	*P* value
Free	27	81.8%	12	66.7%	39 (76.5%)	0.508
Invasive residual	4	12.1%	4	22.2%	8 (15.7%)	
Superficial residual 2	6.1%	2	11.1%	4 (7.8%)		

^Fisher's Exact test was used; **P*-value <0.05 was significant

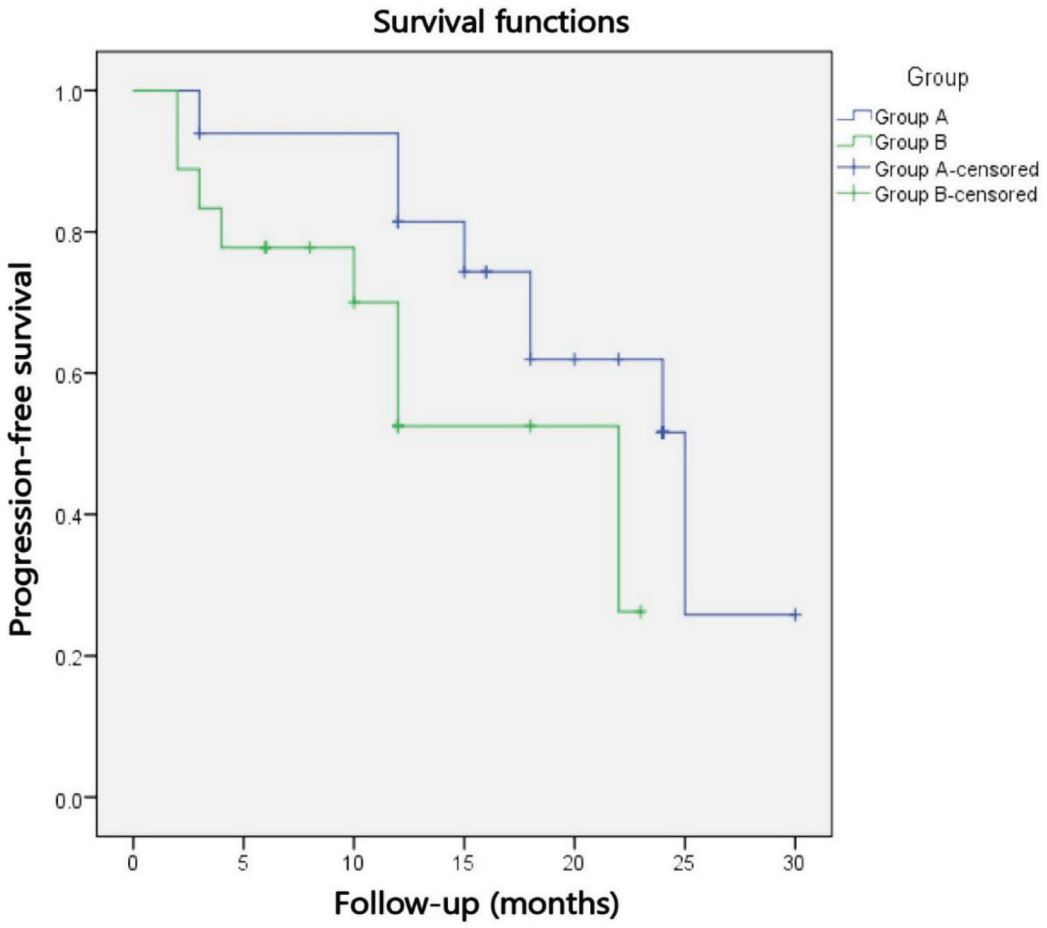


Figure 3. This figure shows the progression-free survival time that was significantly higher in groups A (bladder only radiation) and B (whole pelvic radiation).

Table 4. Incidence of local recurrence in both study groups A (bladder only radiation) and B (whole pelvic radiation)

Local recurrence	Group A		Group B		*P* value
	N	%	N	%	
Yes	2	7.4%	1	8.3%	
No	25	92.6%	11	91.7%	
Total	27		12		0.99

N: Number

Table 5. Comparable toxicity profile in patients of both study groups A (bladder only radiation) and B (whole pelvic radiation)

Variable	Group A N = 33		Group B N = 18		Total N = 51 N (%)	*P*-value
	N	%	N	%		
Bladder toxicities^						
G1	26	78.7%	10	55.6%	36 (70.6%)	0.045*
G2	5	15.2%	2	11.1%	7 (13.7%)	
G3	2	6.1%	6	33.3%	8 (15.7%)	
Intestine^						
No	9	27.3%	1	5.6%	10 (19.6%)	
G1	24	72.7%	8	44.4%	32 (62.7%)	<0.001*
G2	-	-	9	50%	9 (17.6%)	
Rectum^						
No	4	12.1%	1	5.6%	5 (9.7%)	
G1	25	75.8%	11	61.1%	36 (70.6%)	0.209
G3	4	12.1%	6	33.3%	10 (19.6%)	

^Fisher's exact test was used; **P*-value <0.05 was significant; N: Number

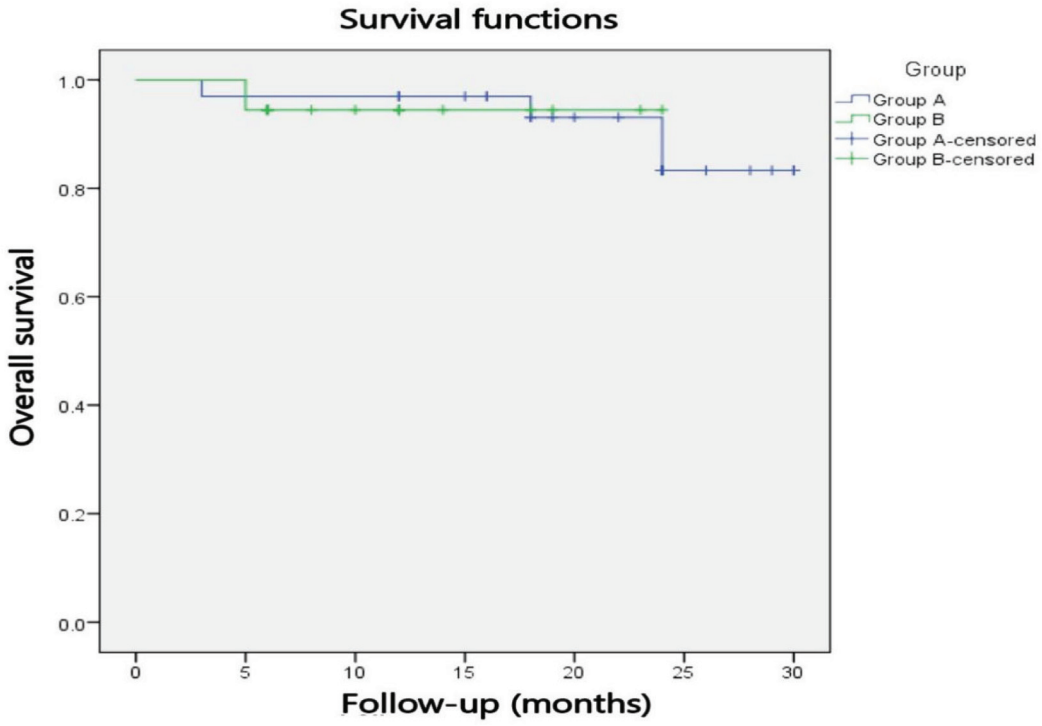


Figure 4. This figure shows the overall survival for the studied bladder cancer patients.

Table 6. Mean and median values for progression-free survival time of the studied bladder cancer patients

	Mean survival time	Standard error	Median survival time	Standard error	*P*-value
Group A	21.65	1.64	25.00	3.67	0.034*
Group B	15.30	2.08	22.00	5.43	

**P*-value <0.05 was significant

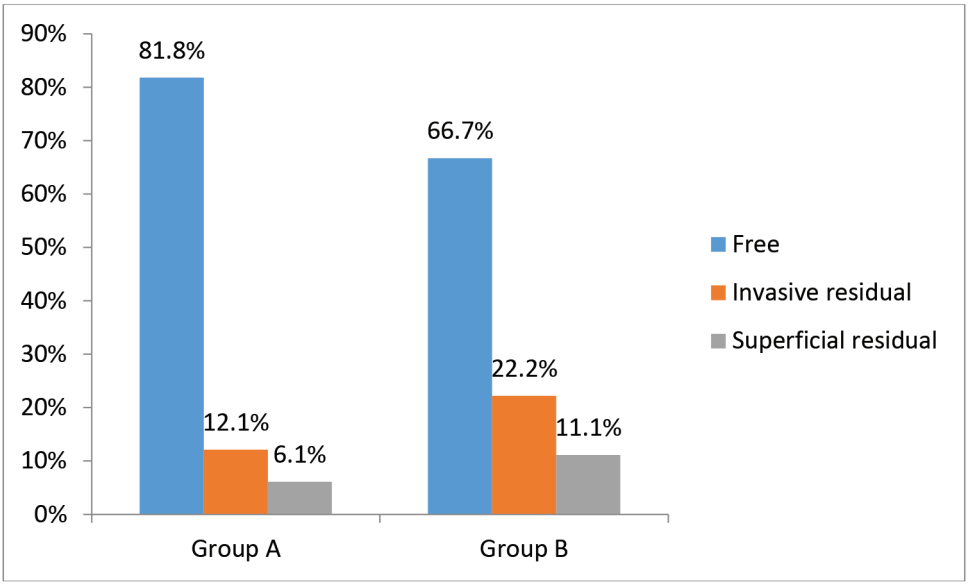


Figure 5. This figure shows the response to treatment among the studied bladder cancer patients. Group A (bladder only radiation) and Group B (whole pelvic radiation)

one patient had locoregional (T3 and G2 nodal outside radiation field) (Table 4).

When both groups were evaluated regarding Toxicity profile, data showed favorable toxicity profile in group A schedule. That emphasize high local control with low Grade intestinal toxicity (no G3 entritis) (Table 5, Figure 2).

- Survival analysis was determined using Kaplan Meier method. Log –rank test was used to compare between survivals of two treatment groups. A *P*-value equal or less than 0.05 was considered significant.

All patients were followed and assessed to compare OS impact. Group A showed significant higher PFS over group B ($P = 0.034$) (Table 6, Figure 3).

Table 6 shows that PFS time was significantly higher in group A than group B ($P = 0.034$).

By statistical point of view, there was no statistically significant difference between mean survival time of group A and group B (28.13 ± 0.97 vs. 22.94 ± 1.03 respectively, $P = 0.952$). That confirm our aim as bladder only radiation field can achieve same local control, non-inferior OS and significant higher PFS. On the other hand, less toxicity profile in bladder only coverage of radiation (Figure 4).

Discussion

In our study, all bladder cancer patients underwent maximum transurethral resection of bladder cancer. Treatment was started within 4-6 weeks after the maximal transurethral resection before randomization. With staging work up according to standard investigation and AJCC, most of cases were Stage III in group A but II and III in group B. Thus, there was no significant difference between groups regarding stage grouping. After assessment of treatment in both groups, 81.8% of Group A achieved CR but 67% in Group B, which is great impact of local control in both groups with non-inferiority of bladder only radiation. Regarding toxicity profile, the data showed favorable toxicity profile in group

A schedule. That emphasize high local control with low Grade intestinal toxicity (no G3 enteritis). All patients were followed and assessed to compare overall survival impact. Group A showed significant higher PFS over group B ($P = 0.034$). No statistically significant difference between mean survival time of group A and group B (28.13 ± 0.97 vs. 22.94 ± 1.03 respectively, $P = 0.952$). That is confirm our aim as bladder only radiation field can achieve same local control, non-inferior OS and significant higher PFS. On the other hand, less toxicity profile in bladder only coverage of radiation.

Trimodality treatment (TUBRT then chemoradiotherapy) in combination or sequentially has been accepted by consensus as a standard option for a bladder preserving strategy. Using four fields conformal radiotherapy, based on two phases technique, have to irradiate gross tumor, whole bladder and pelvic LN in first phase. Then, the 2nd phase has to boost gross tumor only. Micrometastasis of LN despite negative imaging is a well-recognized problem in patients with solid malignancies including prostate, lung, and breast cancers, and prophylactic LN irradiation has shown survival benefits.[5]

Initial bladder-preserving trials recommended pelvic LN treatment, based on historic data of cystectomy series showing up to 18%-40% risk of micrometastases in PLNs for clinical T2−4N0 tumors treated without neoadjuvant chemotherapy.[6] The Radiation Therapy Oncology Group (RTOG) cooperative trials were pioneer in establishing bladder-preserving chemoradiation for MIBC in the US, historically used a mini-pelvis treatment volume covering the iliac lymph nodes up to the mid-sacrum.[7]

In the present study, the patients were randomly assigned to chemoradiation with approved clinical staging cT2-4, N0 (upon MRI finding and cystescopy. During treatment, all patients passed the same assessment protocol and toxicity evaluation. An analysis of patients demographic characteristics showed that no significant difference between both groups. The mean age in groups A and B was 59.42 ± 9.63 and 61.78 ± 11.21. Also, 97% of patients in Group A and 90% of patients in Group B were male. Also, 75% of the patients had TCC. Regarding TNM, most of cases were T2 (52% in Group A, 61% in Group B). At the end of chemoradiation, all patients were assessed to response and meet CR in 81.8%, 66.7%, respectively. Those who suffered from residual disease passed though repeated TURT in 7.8% of all patient as achieving superficial residual and no LN recurrence in all cases (Figure 5). It is presented in many trials by Tunio et al. for MIBC conservative treatment as 18 (18.9%) patients in the whole pelvis concurrent chemoradiation (WP-CCRT) group and 19 (20.9%) patients in the bladder only concurrent chemoradiation (BO-CCRT) group had superficial bladder cancers (pT1, G2) who underwent maximal TURBT and intravesical bacille Calmette-Guerin. These patients were assigned for bladder preservation.

Mutahir A. et al. analysed patients of concurrent CRT, randomly assigned to WP-CCRT (120 patients) and BO-CCRT (110 patients). The CR rates at 3 months were similar between the two groups: 95 patients (93.1%) (95% confidence interval (CI), 100) in the WP-CCRT group and 91 patients (92.8%) (95% CI, 83-100) in the BOCCRT group ($P = 0.3$). All patients with partial response, 7 cases in each group (had residual muscle invasive cancer), referred to salvage cystectomy. Despite a lower theoretical risk of missing the mobile target (i.e., bladder) by larger WP-CCRT, there was no significant difference in intravesical and locoregional recurrence between the two groups. It was difficult to identify an advantage of pelvic nodal irradiation in patients. It explains why some patients cannot benefit because their risk of occult LN metastasis is too low, whereas others may not benefit because their risk of systemic metastasis is too high.[8]

Regarding toxicity profile, both groups analysis showed comparable G2 bladder toxicity but group B patients suffered of higher G3 cystitis 33%. On the other hand, G2 enteritis was observed in majority of whole pelvic irradiation (50%) ($P = 0.001$). That is explaining the impact of intestinal volume included in pelvic field of radiation. As presented in Mutahir A. et al. study, the overall

incidence of Grade 3 or 4 acute toxicity during the CCRT was 17.6% in the WP-CCRT group and 13.3% in the BOCCRT group (P = 0.05). Grade 3 or 4 acute gastrointestinal toxicity was documented less in the BO-CCRT group than in the WP-CCRT group.

Expanded radiation treatment fields to include the PLNs expected to impact local control; however, not mortality. As micrometastatic lymph node harbor high risk to disseminated metastases which negate any improved pelvic disease control achieved with PLN radiation, or that salvage therapy in the proportion of cases that had pelvic nodes recur that may have decreased survival. Analysis of MIBC patients who underwent cystectomy, showed 40% LN secondaries if received no chemotherapy. Using neoadjuvant chemotherapy proved to decrease LN metastasis to <20%.[9] Unfortunately, BC2001 trial reported 5% of patients passed complete concomitant chemoradiation (5 fluorouracil and mitomycin C) regimen.[10]

Finally, radiation technique plays a key role as ideal radiation treatment fields with 3D conformal radiotherapy (3DCRT) should include generous margins surrounding CTV to compensating daily setup and penumbra. Treated volume could involve a substantial part of perivesicular, obturator, and internal iliac lymph nodes.[11]

In BC2001, all MIBC patients treated with bladder-only field 3DCRT technique. Actually, 3DCRT is more frequently used in patients receiving bladder only vs bladder plus PLN radiation. In case of nodal positive, improved pelvic control with pelvic nodal irradiation may increase a survival benefit through locoregional cancer control. On the other hand, elective to lymph nodes irradiation may attenuate anti-tumor immune response via restrained chemokine expression and immune reaction to tumor. Whether elective nodal irradiation adversely affect the impact of immunotherapy for MIBC remains unknown.[12]

All patients were assessed during chemoradiation, most of group A suffered from G1 cystitis (79%) but higher G 3 toxicity 33% in Group B. Also, G2 enteritis was high in Group B (50%) presented in one randomized trial that comparing bladder only vs whole pelvis chemoradiation showed significantly higher rates of grade 3+ acute toxicity, with prominent differences in gastrointestinal toxicity such as diarrhea.[13] The study reported high grade toxicity in MIBC patients assigned to radiosensitizer agents as gemcitabine, mitomycine or 5 Fluorouracil.[14]

As old chemoradiation protocols used to add more toxicity via large pelvic radiation fields, multidisciplinary team recommendations is of great impact to select convenient bladder preservation schedules to MIBC. PFS in group A significantly improved over group B with HR of 0.25. Of all survived patients in group A, 5 patients relapsed. Two patients had local recurrence only. One patient had bone metastasis in spite of free locally. Other 2 patients had local and distant visceral metastasis.

Analysis of group B: Three patients suffered from disease recurrence (local or distant). One patient had pelvic bone metastasis after the end of chemoradiation for which patient received CT (cisplatin and gemcitabine for 3 cycles). Two patients had persistent local MIBC and developed distant metastasis.

All patients of study had been followed by routine cystoscopy and MRI which had false negative result with new positron emission tomography scan updates, recommend to be included in follow-up to increase the accuracy of response and relapse detection. This was the main limitationwe met during data collection.

Conclusion

Bladder-only chemo radiation has non-inferior local control of node-negative bladder cancer with significantly higher PFS. The pelvic nodal radiation field has an unfavorable toxicity profile (higher G2 enteritis).

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Authors' Contribution

All authors contributed to study concepts and design; WAA, NAA. Contributed to case recruitments, interpretation and analysis. All authors contributed to literature research, manuscript drafting, revision and editing. All authors read and approved the final manuscript.

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Conflict of Interest

None declared.

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