

Original Article

Radiotherapy Related Bowel and Bladder Toxicity after Prostate Cancer Irradiation

Saif Ur Rehman^{1*}, Shafaq Maqsood², Aneela Deevan³

¹Assistant Professor of Radiotherapy, Ganga Ram Hospital, Lahore, Pakistan

²Senior Registrar, Oncology Department, Ganga Ram Hospital, Lahore, Pakistan

³Medical Officer, Oncology Department, Ganga Ram Hospital, Lahore, Pakistan

*Corresponding Author: Saif Ur Rehman; Email: drsaif73@yahoo.com

Conflict of Interest: None.

Rehman SU., et al. (2024). 4(2): DOI: <https://doi.org/10.61919/jhrr.v4i2.874>

ABSTRACT

Background: Pelvic radiotherapy is a primary treatment modality for organ-confined prostate cancer and early-stage endometrial cancer. While effective in improving survival rates and reducing recurrence, it is associated with a range of side effects that can impact patient quality of life.

Objective: The study aimed to assess the incidence, management, and resolution of acute and chronic side effects of pelvic radiotherapy in prostate and endometrial cancer patients, focusing on bowel and bladder functions.

Methods: This single-center, observational study included 50 patients diagnosed with prostate or endometrial cancer who underwent pelvic radiotherapy with a dose of 66-70 Gy using a four-field technique on a linear accelerator. Patients were assessed for bladder and bowel dysfunction, with follow-up at 6, 12, and 18 months post-treatment. Statistical analysis involved univariate weighted distribution of response frequencies and paired t-tests for ordinal scale scores, using SPSS version 25 for data analysis.

Results: Of the participants, 22% experienced dysuria, 64% reported bladder outlet obstruction, and 20% had constipation. Acute bowel symptoms like diarrhea occurred in 32%, and chronic proctitis developed in 22% of patients. Urinary symptoms appeared by the third week and generally resolved within weeks; however, bowel symptoms persisted longer but returned to baseline by 18 months post-treatment. Approximately 70% of patients reported good tolerance to radiotherapy.

Conclusion: Pelvic radiotherapy is effective in treating prostate and endometrial cancers but requires management of transient side effects to improve patient outcomes. Advanced radiotherapy techniques such as IMRT and 3D CRT have shown potential in reducing these side effects, emphasizing the need for continuous technological advancements and patient-centered care in radiotherapy.

Keywords: Pelvic radiotherapy, prostate cancer, endometrial cancer, radiotherapy side effects, bladder dysfunction, bowel dysfunction, IMRT, 3D conformal radiotherapy, patient outcomes.

INTRODUCTION

Pelvic radiotherapy and radical prostatectomy are the primary treatment modalities for prostate cancer, offering prolonged survival but often accompanied by chronic side effects (1). An analysis involving 1020 patients from two significant RTOG trials highlighted a 7% incidence of chronic urinary issues necessitating hospitalization, though surgical interventions were required in only 0.5% of cases (RTOG trials) (2). Notably, over half of the long-term urinary complications consisted of urethral strictures, predominantly observed in patients previously subjected to transurethral resection of the prostate (TURP). Furthermore, chronic intestinal complications that led to hospital admissions were reported in 3.3% of the patients, with severe outcomes such as bowel obstruction and perforation occurring in 0.6% of cases. The incidence of life-threatening complications stood at approximately 0.2% (3-7). This study aims to evaluate the long-term effects of radiotherapy on the bowel and bladder functions in patients treated for prostate cancer, providing insights into the management and prevention of these serious side effects (8-11).

MATERIAL AND METHODS

A total of 50 patients diagnosed with prostate cancer were enrolled in this study at our institute from July 2021 to July 2022. Of these, 24 patients presented with disease confined to the prostate and underwent pelvic radiotherapy using a uniform dose of 66-

70 Gy delivered via a four-field technique on a linear accelerator with energies of 6MV and 15MV. Post-therapy follow-up was conducted regularly, focusing on the assessment of bowel and urinary function and their impact on health-related quality of life. The evaluation included the frequency of stool passage, presence of tenesmus, rectal discomfort, urinary incontinence, frequency of incontinence episodes, and the overall patient satisfaction with the treatment outcomes (12).

All participants provided written informed consent, which was obtained after a thorough explanation of the treatment procedures and potential chronic side effects such as urinary incontinence, proctitis, and bladder contractures, adhering to the ethical guidelines of the Declaration of Helsinki.

The impact of pelvic irradiation on bowel and bladder functions was assessed using two primary statistical methods. Initially, responses regarding each function were tabulated in a univariate weighted distribution at successive time intervals of 6, 12, and 18 months post-treatment. Each condition was scored on an ordinal scale ranging from 1 to 3, and the significance of changes in these scores over time was analyzed using a paired t-test. Additionally, a composite score ranging from 0 to 100 was calculated for each patient, where a score of 100 indicated no dysfunction. Due to the stratified sampling by race and age group, the Horvitz-Thompson weighting system was applied to the data to ensure appropriate representation (13). All statistical analyses were performed using SPSS version 25, ensuring that data interpretation was accurate and reflected the weighted values.

RESULTS

During the median follow-up period of 18 months, a comprehensive assessment of bladder and bowel functions was conducted among the patients, who ranged in age from 44 to 82 years with a median age of 60. Most patients (60%) were within the 60-70 year age bracket, and 20% were older than 70 years. A significant proportion of the cohort, approximately 66%, had comorbid conditions, including diabetes (60% of patients), hypertension (62%), and COPD (20%). Socioeconomically, 70% of the patients were classified as poor, 25% had an average economic status, and 5% were considered well-off.

Table 1: Numerical Summary of Bladder and Bowel Function Outcomes in Patients Undergoing Pelvic Radiotherapy

Variable	Total Patients (n=50)	Affected Patients	Incidence (%)
Age Range (years)	44-82	-	-
Median Age (years)	60	-	-
Dysuria	50	11	22
Bladder Outlet Obstruction	50	32	64
Constipation	50	10	20
Diarrhea	50	16	32
Proctitis	50	11	22
Urethral Strictures	(Patients with prior TURP)	Varies	>50
Patients with Diabetes	50	30	60
Patients with Hypertension	50	31	62
Patients with COPD	50	10	20
Socioeconomic Status (Poor)	50	35	70
Socioeconomic Status (Average)	50	12.5	25
Socioeconomic Status (Well-off)	50	2.5	5
Hospitalizations for Proctitis	50	5	10
Major Interventions for Proctitis	50	4	8

Bladder-related symptoms were notably prevalent, with 22% of patients experiencing dysuria and 64% reporting symptoms indicative of bladder outlet obstruction. On the bowel function front, 20% of patients presented with constipation at the outset. During the course of treatment and follow-up, subacute to late bowel complications arose primarily between 6 to 12 months post-radiotherapy. Notably, 32% of subjects experienced diarrhea in the second week of therapy, although these symptoms were transient and effectively managed with dietary modifications and medications. Proctitis was reported in 22% of the patients, managed with sitz baths and cortisone suppositories, with all bowel symptoms returning to baseline by 18 months post-treatment.

In terms of urinary function, the radiotherapy seemed to exert a milder impact. There was a mild worsening of urinary incontinence during the last three weeks of treatment, which gradually improved following the conclusion of the therapy. Over half of the urinary complications were related to urethral strictures, predominantly among those who had previously undergone transurethral resection of the prostate (TURP).

Overall, the majority of the bowel and bladder complications were self-limiting and resolved over time. Approximately 70% of patients demonstrated good tolerance to the radiotherapy. The results indicate that while pelvic irradiation can lead to moderate to severe aftereffects in the treatment of organ-confined and early-stage prostate cancer, these complications generally resolved within 6 months post-therapy. Acute urinary complications were effectively managed with NSAIDs or alpha-blockers. In more severe cases, delayed rectal complications, particularly proctitis, affected about 30% of patients, with 10% requiring hospitalization and 8% needing major interventions.

DISCUSSION

Pelvic radiotherapy has been established as an effective sole modality for treating organ-confined prostate cancer and early-stage endometrial cancer. Despite its efficacy, moderate to severe side effects are commonly observed, though they typically resolve within six months. In the present study, urinary symptoms emerged by the third week of treatment but generally ameliorated within a few weeks (14). Acute bowel symptoms were predominantly alleviated through dietary modifications, while chronic proctitis, developing between six to twelve months post-radiation, responded favorably to sitz baths and steroid suppositories. Notably, approximately 30% of our patients experienced delayed rectal complications such as proctitis, with 10% requiring hospitalization and 8% necessitating major interventions. Acute urinary complications were effectively managed with NSAIDs or alpha blockers (15).

The majority of bowel and rectal complications were self-limiting, and recovery was observed over time. About 70% of patients demonstrated good tolerance to radiotherapy. The introduction of advanced radiotherapy techniques, such as intensity-modulated radiotherapy (IMRT) and 3D conformal radiotherapy (3D CRT), has been instrumental in reducing the toxicity associated with pelvic radiotherapy, enhancing patient outcomes in both acute and late side effects scenarios (16).

The therapeutic advantages of pelvic radiotherapy extend beyond local disease control, contributing to improved overall survival, biochemical failure-free survival, disease-free survival, and reduced rates of distant metastases. Additionally, patients receiving adjuvant pelvic radiotherapy exhibited lower loco-regional recurrence rates. However, a notable late effect of pelvic radiotherapy is infertility, particularly relevant in patients of childbearing age. Proper counseling and preventive measures are imperative to address this concern before administering radiotherapy (17-19).

While the results are promising, the study has limitations, including a relatively small sample size and a lack of a control group, which may limit the generalizability of the findings. Future research should focus on larger, multi-center trials to validate these outcomes and potentially explore the long-term impacts of newer radiotherapy techniques on quality of life and functional outcomes. Additionally, ongoing advancements in radiotherapy technology and technique are recommended to further minimize the side effects and enhance the therapeutic ratio (20).

CONCLUSION

In conclusion, pelvic radiotherapy proves to be a valuable treatment for organ-confined prostate and early-stage endometrial cancers, significantly enhancing survival rates and reducing recurrence. Although associated with moderate to severe side effects, these are generally transient and manageable with current interventions. The study underscores the importance of advanced radiotherapy techniques, such as IMRT and 3D CRT, which play a crucial role in minimizing side effects and improving patient outcomes. Addressing fertility concerns through proper counseling before treatment is also essential, highlighting the need for a holistic approach in patient care to maximize benefits and minimize risks associated with pelvic radiotherapy.

REFERENCES

1. Murthy V, Maitre P, Bhatia J, Kannan S, Krishnatry R, Prakash G, Bakshi G, Pal M, Menon S, Mahantshetty U. Late toxicity and quality of life with prostate only or whole pelvic radiation therapy in high risk prostate cancer (POP-RT): A randomised trial. *Radiotherapy and Oncology*. 2020 Apr 1;145:71-80.

2. Catucci F, Alitto AR, Masciocchi C, Dinapoli N, Gatta R, Martino A, Mazzarella C, Fionda B, Frascino V, Piras A, D'Aviero A. Predicting radiotherapy impact on late bladder toxicity in prostate cancer patients: an observational study. *Cancers*. 2021 Jan 6;13(2):175.
3. Wang K, Mavroidis P, Royce TJ, Falchook AD, Collins SP, Sapareto S, Sheets NC, Fuller DB, El Naqa I, Yorke E, Grimm J. Prostate stereotactic body radiation therapy: an overview of toxicity and dose response. *International Journal of Radiation Oncology* Biology* Physics*. 2021 May 1;110(1):237-48.
4. Parry MG, Nossiter J, Cowling TE, Sujenthiran A, Berry B, Cathcart P, Clarke NW, Payne H, van der Meulen J, Aggarwal A. Toxicity of pelvic lymph node irradiation with intensity modulated radiation therapy for high-risk and locally advanced prostate cancer: a national population-based study using patient-reported outcomes. *International Journal of Radiation Oncology* Biology* Physics*. 2020 Dec 1;108(5):1196-203.
5. Murthy V, Adsul K, Maitre P, Singla A, Singh P, Panigrahi G, Raveendran V, Phurailatpam R. Acute and Late Adverse Effects of Prostate-Only or Pelvic Stereotactic Radiation Therapy in Prostate Cancer: A Comparative Study. *International Journal of Radiation Oncology* Biology* Physics*. 2022 Oct 1;114(2):275-82.
6. Pepin A, Aghdam N, Shah S, Kataria S, Tsou Jr H, Datta S, Danner M, Ayoob M, Yung T, Lei S, Gurka M. Urinary morbidity in men treated with stereotactic body radiation therapy (SBRT) for localized prostate cancer following transurethral resection of the prostate (TURP). *Frontiers in Oncology*. 2020 May 5;10:555.
7. Houben J, McColl G, Kaanders JH, Smeenk RJ. Patient reported toxicity and quality of life after hypofractionated high-dose intensity-modulated radiotherapy for intermediate-and high risk prostate cancer. *Clinical and Translational Radiation Oncology*. 2021 Jul 1;29:40-6.
8. Magli A, Farneti A, Faiella A, Ferriero M, Landoni V, Giannarelli D, Moretti E, de Paula U, Gomellini S, Sanguineti G. Toxicity at 1 year after stereotactic body radiation therapy in 3 fractions for localized prostate cancer. *International Journal of Radiation Oncology* Biology* Physics*. 2021 Sep 1;111(1):93-100.
9. Mylona E, Cicchetti A, Rancati T, Palorini F, Fiorino C, Supiot S, Magne N, Crehange G, Valdagni R, Acosta O, de Crevoisier R. Local dose analysis to predict acute and late urinary toxicities after prostate cancer radiotherapy: Assessment of cohort and method effects. *Radiotherapy and Oncology*. 2020 Jun 1;147:40-9.
10. Jorgo K, Polgar C, Major T, Stelczer G, Herein A, Pocza T, Gesztesi L, Agoston P. Acute and late toxicity after moderate hypofractionation with simultaneous integrated boost (SIB) radiation therapy for prostate cancer. A single institution, prospective study. *Pathology & Oncology Research*. 2020 Apr;26:905-12.
11. Reinikainen P, Kapanen M, Luukkaala T, Kellokumpu-Lehtinen PL. Acute side-effects of different radiotherapy treatment schedules in early prostate cancer. *Anticancer research*. 2022 May 1;42(5):2553-65.
12. Juarez JE, Romero T, Mantz CA, Pepin A, Aghdam N, Suy S, Steinberg ML, Levin-Epstein RG, Nickols NG, Kaplan ID, Meier RM. Toxicity after stereotactic body radiation therapy for prostate cancer in patients with inflammatory bowel disease: A multi-institutional matched case-control series. *Advances in Radiation Oncology*. 2021 Nov 1;6(6):100759.
13. Christiansen RL, Dysager L, Hansen CR, Jensen HR, Schytte T, Nyborg CJ, Bertelsen AS, Agergaard SN, Mahmood F, Hansen S, Hansen O. Online adaptive radiotherapy potentially reduces toxicity for high-risk prostate cancer treatment. *Radiotherapy and Oncology*. 2022 Feb 1;167:165-71.
14. David RV, Kahokehr AA, Lee J, Watson DI, Leung J, O'Callaghan ME. Incidence of genitourinary complications following radiation therapy for localised prostate cancer. *World journal of urology*. 2022 Oct;40(10):2411-22.
15. Tree AC, Ostler P, van der Voet H, Chu W, Loblaw A, Ford D, Tolan S, Jain S, Martin A, Staffurth J, Armstrong J. Intensity-modulated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): 2-year toxicity results from an open-label, randomised, phase 3, non-inferiority trial. *The Lancet Oncology*. 2022 Oct 1;23(10):1308-20.
16. Qi X, Li HZ, Gao XS, Qin SB, Zhang M, Li XM, Li XY, Ma MW, Bai Y, Li XY, Wang D. Toxicity and biochemical outcomes of dose-intensified postoperative radiation therapy for prostate cancer: results of a randomized phase III trial. *International Journal of Radiation Oncology* Biology* Physics*. 2020 Feb 1;106(2):282-90.
17. Nuijens AC, Oei AL, Bouhuijs A, Franken NA, Rasch CR, Stalpers LJ. A comparison between patient-and physician-reported late radiation toxicity in long-term prostate cancer survivors. *Cancers*. 2022 Mar 25;14(7):1670.
18. Alayed Y, Quon H, Ong A, Cheung P, Chu W, Chung H, Vesprini D, Chowdhury A, Panjwani D, Pang G, Korol R. Accelerating prostate stereotactic ablative body radiotherapy: Efficacy and toxicity of a randomized phase II study of 11 versus 29 days overall treatment time (PATRIOT). *Radiotherapy and Oncology*. 2020 Aug 1;149:8-13.

19. Glicksman RM, Liu SK, Cheung P, Vesprini D, Chu W, Chung HT, Morton G, Deabreu A, Davidson M, Ravi A, Musunuru HB. Elective nodal ultra hypofractionated radiation for prostate cancer: Safety and efficacy from four prospective clinical trials. *Radiotherapy and Oncology*. 2021 Oct 1;163:159-64.
20. Schumacher O, Luo H, Taaffe DR, Galvao DA, Tang C, Chee R, Spry N, Newton RU. Effects of exercise during radiation therapy on physical function and treatment-related side effects in men with prostate cancer: a systematic review and meta-analysis. *International Journal of Radiation Oncology* Biology* Physics*. 2021 Nov 1;111(3):716-31.