TURKISH JOURNAL of ONCOLOGY

Turk J Oncol 2024;39(3):274–278
doi: 10.5505/tjo.2024.4363

ORIGINAL ARTICLE

The Penile Bulb Radiation Dose Effect on Urinary Incontinence in Prostate Cancer Patients

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OBJECTIVE

This is the first study to determine whether there is a relationship between penile bulb radiation dose and urinary incontinence.

METHODS

This study comprises 131 patients with localized, locally advanced, and pelvic oligometastatic prostate cancer treated at our institution. All patients were treated with IMRT between February 2016 and August 2020. Urinary incontinence after the treatment was assessed retrospectively using a standardized follow-up program based on data available at our center. The urinary incontinence was scored using the CTCAE version 5.0 scoring system. In univariate analysis, the Mann-Whitney test was used to detect any association between penile bulb V50 doses and membranous urethral length on urinary incontinence.

RESULTS

Urinary incontinence after the treatment was reported in 17 of 131 patients. The average penile bulb V50 values of patients with incontinence were 28.66 gy and 26.8 in patients who did not have urinary incontinence. The mean membranous urethral length was 3.01cm in patients with incontinence and 3.34cm in patients without incontinence. Although these parameters have minimal difference in patients with and without incontinence, they are not statistically significant (p>0.05 all).

CONCLUSION

Radiation-induced urinary incontinence was not associated with the radiation dose of the penile bulb and membranous urethral length. However, further studies are essential.

Keywords: Intensity-Modulated Radiotherapy (IMRT); membranous urethra; penile bulb; prostate cancer; urinary incontinence.

INTRODUCTION

The use of radiation therapy to treat prostate cancer inevitably involves exposure of normal tissues. As a result, patients may experience symptoms associated with damage to normal tissue after the therapy. Urinary incontinence is one of the most clinically relevant side effects in the treatment of prostate cancer patients.[1]

There are many known anatomical and physiological parameters related to urinary continence. Rehder et al.[2] described the effect of the penile bulb on urinary continence for the first time. This was based on the idea that physiological contraction of the bulbospongiosus muscle increases pressure in the bulb of the penis (as blood is not compressible) and consecutively leads to additional contraction of the urethral lumen. Based on this knowledge,

Received: May 24, 2024
Accepted: June 03, 2024
Online: June 27, 2024

Accessible online at:
www.onkder.org

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a well-vascularized penile bulb is important to erectile function and urinary continence. There are several clinical studies that support this view.[3,4] These studies are about the relationship between continence surgery and male sexual function. No study has yet evaluated the penile bulb radiation dose effect on continence.

As we know, radiation treatment affects normal tissue vasculature near the target volume. We searched about the effect of this damage on the penile bulb and related urinary incontinence.

MATERIALS AND METHODS

This retrospective cohort study was composed of 131 patients with localized, locally advanced, and pelvic oligometastatic prostate cancer (excluding distant metastasis). Genitourinary (GU) toxicity was assessed using a standardized follow-up program retrospectively. The GU toxicity endpoints were scored using the Common Terminology Criteria for Adverse Events version 5.0 (CTCAE 5.0) scoring system. The full bladder, different anatomical subregions within the bladder, penile bulb, and membranous urethral length (MUL) were delineated on computed tomography simulation (CT-sim).

Patients

This retrospective cohort study was composed of 131 patients with localized, locally advanced prostate cancer and pelvic oligometastatic disease. We excluded extrapelvic-distant metastatic prostate cancer patients from the study. All patients were treated with radiotherapy between February 2016 and August 2020. Of the 131 patients, 30 were those who had undergone radical prostatectomy (salvage prostatectomy was excluded). Urinary incontinence that occurred after the treatment was evaluated. Radiotherapy was delivered using linear accelerators with 6 MV photons by intensity-modulated radiotherapy (IMRT). Patients were treated five times per week at doses ranging from 66 to 76 Gy at the planning target volume (PTV) using a standard 2 Gy per fraction. Six of the patients consisted of those treated with the hypofractionated regimen (2 Gy < per fraction). In the current patient cohort, 36.6% of patients had irradiated pelvic lymph nodes as part of therapy. Setup accuracy was verified during delivery by matching bony anatomy. Most patients with locally advanced prostate cancer received adjuvant hormonal treatment. Diabetes, hypertension, coronary artery disease, and peripheral artery disease were defined as 'vascular diseases'. Other diseases, such as endocrinological and rheumatological, were described as 'other than vascular disease'. These patient characteristics were retrospectively assessed from detailed patient charts (Table 1).

Target and Organ at Risk Delineation

The high-risk clinical target volume (HR-CTV) consisted of the prostate with or without the SV, depending on the estimated risk of SV invasion. Due to the risk of locoregional metastases, pelvic lymphatics are included in the low-risk clinical target volume (LR-CTV). The full bladder was applied as part of the treatment planning. Patients were instructed to urinate and drink half or one liter of water one hour before the radiotherapy. The penile bulb contouring was done with the ESTRO-ACROP guidelines.[5] The bladder was created using the entire bladder. The trigone was defined as the triangle-shaped structure between the transition of the ureters in the bladder wall cranially and the transition of the urethra into the bladder wall caudally.[6] MUL was measured in the midline sagittal plane on CT-sim. On CT-sim with non-operated patients, MUL was considered to be the distance from the prostatic apex to the level of the urethra at the penile bulb (Fig. 1). With operated patients, MUL was supposed to be the distance from the bladder neck to the layer of the urethra at the penile bulb.[7]

Endpoints

The grade of urinary incontinence according to CTCAE v5.0 was evaluated retrospectively using available patient data between 2016 and 2020. Urinary incontinence grade 1 was defined as occasional leaking (e.g., with coughing, sneezing, etc.) when pads were not indicated, while grade 2 was defined as spontaneous leaking when pads were indicated. In addition, the operation intervention is only applied to grade 3. Urinary incontinence was evaluated for the first six months after treatment. Late urinary incontinence and recovery of incontinence were not evaluated.

Statistical Analysis

In univariate statistical analysis, the Mann-Whitney test was used to detect any association between penile bulb V50-V60 doses and membranous urethral length on urinary incontinence. Besides, the variables of age, comorbidity, operation, hormone therapy, bladder, and trigonum doses were compared to perform a univariate analysis. p value < 0.05 was considered significant. The statistical analysis was performed using IBM SPSS 22.0.

RESULTS

Urinary incontinence after the treatment was reported in 17 of 131 patients. Sixteen of them were grade 1–2

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Table 1 Patient and treatment characteristics

Category		n	%
Treatment related factor	Radikal prostatectomy	30	22.9
	Adjuvant hormonal therapy	102	77.3
Pre-treatment factor	Vascular diseases	55	41.7
	Other than the vascular diseases	6	4.6
	TUR-P	12	9.1
Gleason	6	48	36.6
	7	55	42.0
	8–10	28	21.4
Tumor classification	T1	47	35.9
	T2	62	47.3
	T3	22	16.8
PSA	<4	4	3.1
	4–10	37	28.2
	>10	90	68.7
Age	<70 years	68	51.9
	≥70 years	63	48.1

n: Number of patients; TUR-P: Transurethral resection of the prostate; PSA: Prostate specific antigen

Table 2 Urinary incontinence related parameters

Parameters	Patients without incontinence	Patients with incontinence	p
Penile bulb radiation doses			
Mean	31.32 Gy	31.21 Gy	>0.05
V50	26.8%	28.66%	>0.05
Max	48.04 Gy	49.99 Gy	>0.05
External urethral sphincter radiation doses			
Mean	67.36 Gy	71.32 Gy	>0.05
Bladder trigonum radiation doses			
Mean	71.84 Gy	71.20 Gy	>0.05
V70	80.13%	75.83%	>0.05
V75	32.93%	24.06%	>0.05
Bladder radiation doses			
V55	26.54%	34.10%	>0.05
V65	16.9%	24.25%	>0.05
Urethral length	3.34	3.01	>0.05
Radikal prostatectomy			0.021

incontinence. Grade 3 incontinence was reported in one patient. This patient belonged to the group of patients who had undergone a radical prostatectomy. No grade 4–5 incontinence was reported. The penile bulb V50 values and membranous urethral length were evaluated in the univariate analysis. In the study, the average penile bulb V50 values of patients with incontinence were 28.66. In addition, the penile bulb V50 doses were 26.8 in patients who did not have urinary incontinence. The mean membranous urethral length was 3.01 cm in patients with incontinence and 3.34 cm in patients without incontinence.

Although there is minimal change in these parameters in patients with incontinence, they are not statistically significant (p>0.05 all). The variables of age, comorbidity, operation, hormone therapy, bladder, and trigonum doses were compared to perform a univariate analysis. The only association with incontinence was found with radical prostatectomy (p=0.021) (Table 2).

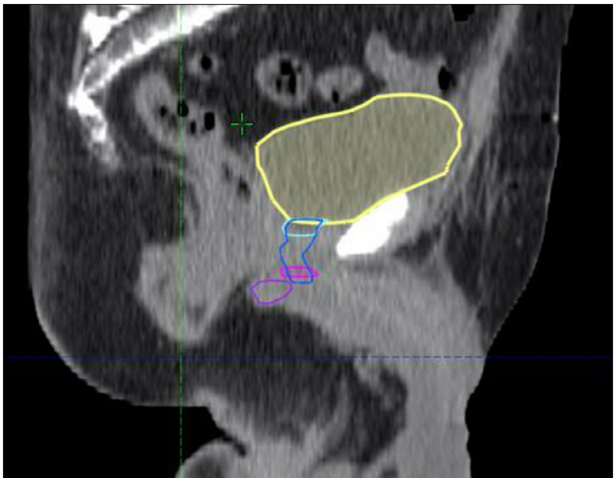

Fig. 1. Sagittal view of the bladder (yellow), trigonum (green), membranous urethra (blue), penile bulb (purple), external and internal sphincters (pink, cyan).

DISCUSSION

Many factors cause urinary incontinence in patients undergoing prostate cancer treatment. One of these is the postoperative membranous urethral length (MUL). Negative impacts on urinary incontinence have been shown in studies.[8–11] These studies have found that MUL is associated with recovery of incontinence. We evaluated this parameter in our study. However, our study did not reach similar results because urinary incontinence recovery was not assessed.

There is an idea that physiological contraction of the bulbospongiosus muscle increases pressure in the bulb of the penis (as blood is not compressible) and consecutively leads to additional contraction of the urethral lumen. A well-vascularized penile bulb is an essential factor in this mechanism. Radiotherapy reduces the blood supply to these anatomic regions, and our study was based on this idea.

The proximal male urethral bulb is an integrated part of the urinary continence mechanism, especially during increased physical activity. Several clinical studies support this view.[3–5] However, these studies have demonstrated that urinary incontinence correlated with sexual function on surgical techniques. No study has yet evaluated the penile bulb radiation dose (sexual function) effect on continence. This study is the first on this aspect.

We have found no relation between urinary incontinence and penile bulb radiation doses. There could be several explanations for this result. The most important one is that we have a short period of follow-up time data retrospectively (six months), so there was no evaluation of late urinary incontinence and recovery. Just like the other factors, it should be kept in mind that penile bulb radiation dose may be associated with incontinence recovery. The second is that we do not use any side effect scoring questionnaires. The clinician's patient records were used for grading urinary incontinence (CTCAE v5.0) retrospectively. This means there may be missing records.

CONCLUSION

Our study showed that there is no relationship between penile bulb radiation dose and urinary incontinence. Besides that, considering the limitations of our study and the studies supporting the correlation between sexual function and urinary incontinence, further studies are essential. We suggest that future studies should be prospective; continence recovery and late urinary incontinence should be examined.

Authorship contributions: Concept – M.A.; Design – M.A., Ş.D.; Supervision – M.A., Ş.D.; Materials – Ş.D.; Data collection and/or processing – Ş.D., M.E.Ş.; Data analysis and/or interpretation – Ş.D.; Literature search – Ş.D.; Writing – Ş.D.; Critical review – M.A., Ş.D.

Conflict of Interest: All authors declared no conflict of interest.

Use of AI for Writing Assistance: Not declared.

Financial Support: None declared.

Peer-review: Externally peer-reviewed.

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