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Large Prostate Volume Predicts Acute Urinary Pain After Prostate SBRT: Threshold Effect Mediated by Bladder Low-Dose Exposure

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ABSTRACT

Purpose Acute urinary pain is common after prostate stereotactic body radiotherapy (SBRT). Although treatment breaks and bladder filling protocols are adopted to mitigate toxicity, evidence supporting these interventions is limited. We investigated the effects of prostate volume, genitourinary dosimetry, treatment timing, and bladder filling on acute urinary pain.

Methods We retrospectively analyzed 118 patients who underwent prostate SBRT. Acute urinary pain was defined as CTCAE v5.0 grade ≥1 within one month. Prostate volume was analyzed continuously (per 10mL) and in quartiles. Bladder, trigone, and urethral dose metrics were evaluated, including the bladder V18Gy (per 10mL). Treatment timing was compared between consecutive daily treatment and treatment with unplanned weekend breaks between fractions. The multivariable logistic regression models included prostate volume, bladder V18Gy, age, baseline IPSS, NCCN risk, medications, bladder filling status, and treatment timing.

Results Urinary pain occurred in 49 patients (41.5%). Prostate volume was significantly associated with pain (OR 1.41 per 10mL, 95%CI 1.15–1.78, p=0.002). Quartile analysis revealed a threshold effect: highest-quartile patients had markedly increased odds versus lowest quartile (OR 4.46, 95%CI 1.24–16.70, p=0.022), with no differences among lower quartiles. Bladder V18Gy was the only dosimetric parameter significantly correlated with prostate volume (Pearson's r=0.41, Spearman's ρ=0.40, p<0.0001). Bladder V18 was associated with urinary pain univariably but lost significance after adjustment, suggesting mediation. Neither weekend treatment breaks nor bladder filling status were independently associated with urinary pain in the multivariable analysis.

Conclusion Large prostate volume strongly predicts acute urinary pain after SBRT, with a non-linear threshold at the upper quartile, mediated by increased bladder low-dose exposure. Despite common clinical practice, neither weekend treatment breaks nor bladder filling protocols independently reduced urinary pain in this cohort. Prostate volume and bladder dosimetry, rather than treatment timing or bladder filling protocols, should guide SBRT planning and patient selection strategies.

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INTRODUCTION

Since May 2021, our institution has implemented CyberKnife®-based prostate SBRT, achieving shortened treatment duration while maintaining excellent local control. Despite these advantages, genitourinary toxicities, particularly acute urinary pain, are relatively common following treatment. In our previous analyses of patients treated with prostate SBRT, several clinical factors—including age, NCCN risk classification, treatment schedule, and bladder filling at treatment—were evaluated as potential predictors of acute urinary pain. However, treatment planning-derived dosimetric factors have not been fully evaluated.

Purpose

In this study, we evaluated prostate volume and dose-volume metrics of the bladder, trigone, and urethra as additional variables and assessed their relationships with acute urinary pain after prostate SBRT.

METHODS AND MATERIALS

Patient Selection

Between May 2021 and March 2025, 118 patients with localized prostate cancer were treated with CyberKnife® SBRT (36.25 Gy in 5 fractions).
Of these, 118 patients with available baseline IPSS, follow-up assessments, and treatment-planning data were included. This study was approved by the institutional review board (IRB) of our institution.

Methods

Clinical variables included prostate volume, age, baseline IPSS, NCCN risk group, lower urinary tract symptom (LUTS) medications, bladder filling at treatment, and treatment schedule (consecutive treatment vs. weekend break). Dosimetric variables included and dose-volume metrics of the bladder, trigone, and urethra (V_{18Gy}, D_{max}, and $D_{0.03cc}$). The primary endpoint was acute urinary pain, defined as CTCAE v5.0 Grade ≥1 within 1 month after SBRT.

Statistical Analysis

Pearson correlations between prostate volume and bladder, trigone, and urethra dose metrics were assessed univariably. Associations with acute urinary pain were evaluated using univariable and multivariable logistic regression analyses.
Multivariable models included prostate volume, bladder V_{18Gy}, age, baseline IPSS, NCCN risk group, medication use, bladder filling at treatment, and treatment schedule. Prostate volume was analyzed as both a continuous variable (per 10 mL) and quartile-based categories. Threshold effects and non-linear relationships between prostate volume and acute urinary pain were also evaluated.

RESULTS

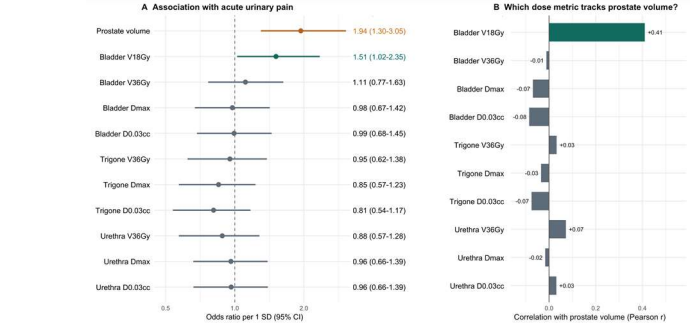

Figure 1. Bladder V_{18Gy} was the only dosimetric parameter associated with acute urinary pain (A) and correlated with prostate volume (B).

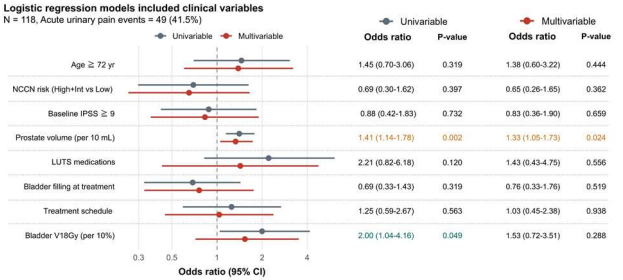

Figure 2. Prostate volume and bladder V_{18Gy} were associated with acute urinary pain in univariable analysis, whereas only prostate volume remained an independent predictor in multivariable analysis.

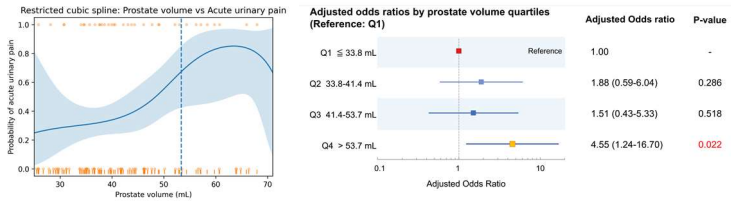

Figure 3. Prostate volume showed a nonlinear threshold effect on acute urinary pain, with a marked increase in risk in the highest quartile.

DISCUSSION

We found that **prostate volume is an important determinant of acute urinary pain** after prostate SBRT. Bladder V_{18Gy} was associated with acute urinary pain, but this association was attenuated after adjustment for prostate volume, suggesting that **increased bladder low-dose exposure may partly mediate this relationship**. These findings are broadly consistent with previous studies showing that prostate volume and urinary dose parameters contribute to urinary toxicity after prostate radiotherapy [1-4].
Neither treatment timing nor bladder filling independently affected urinary pain. Therefore, prostate volume and bladder dosimetry, rather than treatment timing or bladder filling protocols, should guide SBRT planning and patient selection strategies.

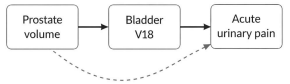

Figure 4. The potential mediating role of bladder dose in the association between prostate volume and acute urinary pain.

CONCLUSIONS

- Large prostate volume was the primary factor associated with acute urinary pain after prostate SBRT.
- The risk increased in patients with larger prostate volumes, suggesting a threshold effect.
- Among the evaluated dose metrics, only bladder V_{18Gy} was associated with acute urinary pain, and this appeared to reflect its correlation with prostate volume.
- Prostate volume may help identify patients at increased risk of acute urinary pain before prostate SBRT.

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