Toxicity following Stereotactic Body Radiotherapy for Prostate Cancer in Patients with Inflammatory Bowel Disease: A Multi-Institutional Matched Case Control Series

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Learning Objective

We aimed to evaluate the safety of stereotactic body radiotherapy for prostate cancer in men with Inflammatory Bowel Disease.

Background

- Stereotactic body radiotherapy (SBRT) is a form of radiotherapy (RT) wherein advanced techniques are used to deliver very large doses of radiation.
- SBRT has been shown to offer favorable efficacy and toxicity outcomes in prostate cancer.
- Inflammatory bowel disease (IBD) is a relative contraindication for RT due to perceived increased risk of bowel toxicity.
- The 2020 National Comprehensive Cancer Network (NCCN) guidelines suggest that inactive Ulcerative Colitis (UC) is a relative contraindication to treatment with RT, while active UC is an absolute contraindication.
- Though many of the studies that established the safety of SBRT explicitly excluded patients with IBD, there are several case-control reports that suggest that other forms of RT, such as conventionally-fractionated RT and brachytherapy, have a reasonable safety profile among patients with IBD.

Methods

- We queried a consortium database for patients with IBD receiving SBRT for prostate cancer between 2006-2012.
- Identified patients were matched with patients without IBD in a 3:1 fashion based on dose, fractionation, use of androgen deprivation therapy, and age distribution (Table 1).
- Logistic regression was used to evaluate the association between having IBD and experiencing acute and late gastrointestinal (GI) and genitourinary (GU) toxicities as scored on the Common Terminology Criteria for Adverse Events scale.
- Time to late toxicity was evaluated using proportional hazard Cox models.

Results

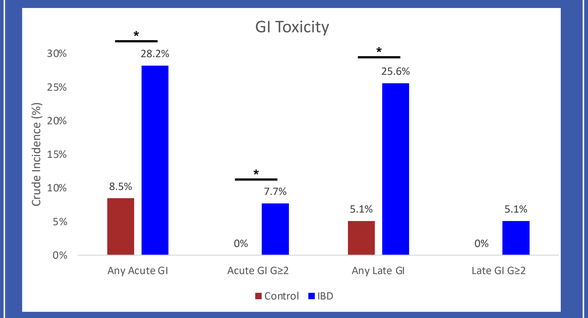
Table 1. Patient and Treatment Characteristics

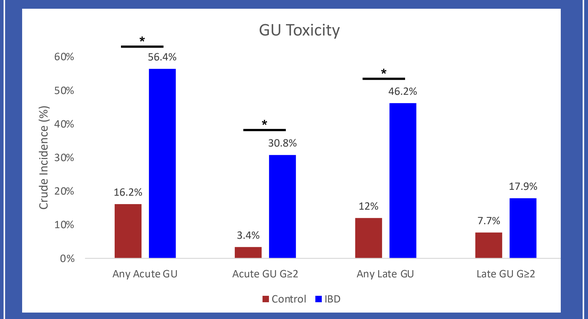
Variable	Control (n = 117)	IBD (n = 39)	P-value
Age at treatment	63 (54-69.9)	65 (60-70)	0.102
Initial PSA	5.9 (4.5-7.8)	5.8 (4.2-8)	0.654
Dose per Fraction			0.001
7	0 (0%)	5 (12.8%)	
7.25	10 (8.5%)	6 (15.4%)	
8	107 (91.5%)	28 (71.8%)	
ADT Use			0.011
No	115 (98.3%)	34 (87.2%)	
Yes	2 (1.7%)	5 (12.8%)	
Follow-up	88.7 (75.6-102)	83.9 (66.8-94.9)	0.152

All patients were treated every other day.

The IBD and control cohorts had median follow-up of 83.9 months (range 66.8-94.9) and 88.7 months (range 75.6-102), respectively.
No patient in the IBD cohort had an active flare at the time of treatment.

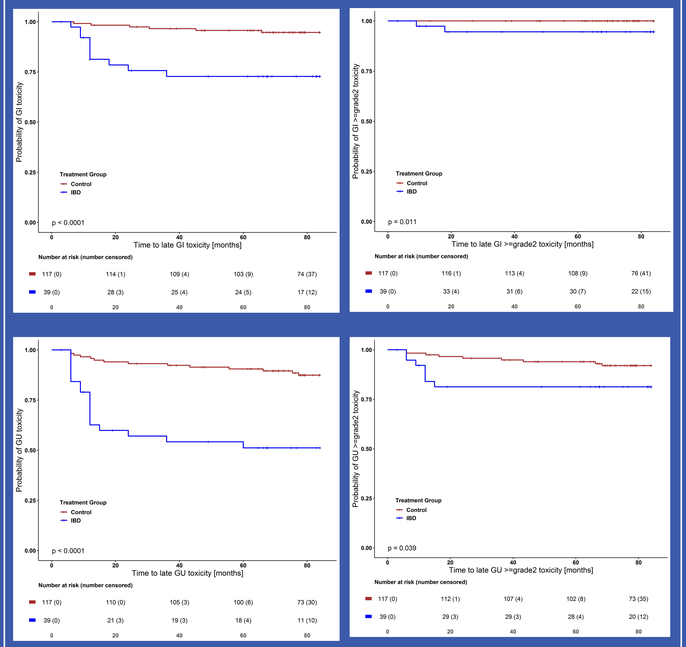
Figure 1. Crude Incidences of Gastrointestinal and Genitourinary Toxicity





Crude incidence of acute grade ≥ 2 GI and GU toxicity were significantly higher in IBD vs control cohort, but there were no differences in crude incidences of late grade ≥ 2 GI and GU toxicities.

Figure 2. Toxicity-Free Survival Curves



There was no significant difference in time to late grade ≥ 2 GI toxicity in patients with IBD, however, patients with IBD had a significantly shorter time to late grade ≥ 2 GU toxicity. Toxicity-free survival was significantly lower in patients with IBD with respect to both late grade ≥ 2 GI and GU toxicities.

Table 2. Unadjusted Logistic Regression for Development of Toxicity in IBD cohort

	OR (95% CI)	P-value
GI Toxicity		
any acute GI	4.13 (1.61,10.59)	0.003
acute GI, grade≥ 2	22.53 (1.12,453.78)	0.042
any late GI	6.11 (2.1,17.77)	<0.001
late GI, grade≥ 2	15.67 (0.72,339.57)	0.08
GU Toxicity		
any acute GU	6.49 (2.92,14.44)	<0.001
acute GU, grade≥ 2	11.47 (3.58,36.70)	<0.001
any late GU	6.14 (2.66,14.18)	<0.001
late GU, grade≥ 2	2.64 (0.93,7.49)	0.069

Association of having IBD and experiencing GI and GU toxicities were evaluated using logistic regression.

Compared to controls, patients with IBD had significantly higher odds of developing acute grade ≥ 2 GI and and acute grade ≥ 2 GU toxicities. However, IBD was not associated with higher odds of late grade ≥ 2 GI or GU toxicities.

Discussion

- Historically, IBD has been considered a contraindication to radiotherapy. Though several previous case-control reports have suggested that other forms of radiation are safe.
- This multi-institutional matched case-control cohort study found that men with IBD who received SBRT for prostate cancer did not have significantly higher odds of late GI or GU grade ≥ 2 toxicity.
- Low grade late GI and GU toxicities were significantly greater and time to toxicity was significantly shorter in the IBD cohort.
- Acute grade ≥ 2 toxicities were also significantly more common among patients with IBD.

Limitations

- Unmeasured bias by treating physicians in recommending RT vs surgery for IBD cohort.
- Difficulty in distinguishing radiation colitis toxicity from the symptoms of IBD flareups.
- Details on immunomodulatory medications and flare-free interval prior to radiation were unavailable.

Conclusion

- Men with IBD who received SBRT for prostate cancer did not have a higher likelihood of developing late grade ≥ 2 GI or GU toxicities.
- Prostate cancer patients with IBD should be counseled about potential toxicity risks but should be offered SBRT as potential treatment option.