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Original article

Patient-reported acute gastrointestinal toxicity in men receiving 3-dimensional conformal radiation therapy for prostate cancer with or without neoadjuvant androgen suppression therapy

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Abstract

Objective: To investigate the impact of 2 months of neoadjuvant and 2 months of concurrent hormonal therapy on the acute gastrointestinal (GI) toxicities associated with 3-dimensional conformal radiation therapy (3D-CRT) for prostate adenocarcinoma.

Methods: The study cohort consisted of 80 men who underwent 3D-CRT with ($n = 40$) or without ($n = 40$) neoadjuvant and concurrent hormonal therapy. Computerized tomography-based planning occurred after neoadjuvant hormonal therapy. All patients completed a previously validated, quality-of-life self-assessment tool on 7 GI symptoms, including diarrhea, urgency, pain, rectal bleeding, cramping, mucus, and tenesmus, at baseline and weekly during radiation therapy.

Results: Patients who received hormonal therapy were more likely to have T2b, T2c, T3a, or T3b ($P < 0.001$) or Gleason score 7, 8, or 9 ($P = 0.02$) disease compared to those that did not. The dose delivered to the planning target volume was 70 Gy for both groups. Median radiation treatment volume was numerically smaller for the hormone group but not to a statistically significant degree (949 vs. 1043 cc, $P = 0.30$). Patients who received hormonal therapy had less rectal pain ($P < 0.01$) and tenesmus ($P = 0.02$) but more rectal mucus ($P = 0.03$) compared to those who did not.

Conclusions: Prostate gland volume reduction after androgen suppression therapy may reduce patient-reported acute GI toxicities associated with 3D-CRT for prostate cancer.

Keywords: Prostate carcinoma; 3-Dimensional conformal radiation therapy; Neoadjuvant hormone therapy; Acute toxicity; Quality of life

1. Introduction

Androgen suppression therapy is commonly used in conjunction with 3-dimensional conformal radiation therapy (3D-CRT) to treat patients with intermediate-risk and high-risk prostate cancer. Several large, randomized clinical trials have shown that androgen deprivation therapy can significantly improve outcomes in patients with locally advanced prostate cancer who are treated with external beam radiation therapy [1–7]. In addition, a recently published trial from the Dana-Farber Cancer Institute showed a benefit to adding 6 months of androgen suppression to conformal, conventional dose radiotherapy in patients with clinically localized prostate cancer [8]. Thus, androgen deprivation therapy will likely remain an integral component of prostate cancer treatment.

Quality-of-life changes that result from treatment are important considerations for patients choosing among various treatment options for prostate cancer. To date, few studies have reported on the effect of adding androgen suppression therapy to conformal radiation in terms of quality-of-life changes experienced by the participants. Most information in this regard has come from large trials that have analyzed toxicity as a secondary outcome. These studies have used physician assessment

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Table 1
Self-administered questionnaire

Please circle the answer for each question that best describes your symptoms:				
1. In the past week, did you have loose, watery stools?				
Never	Once or twice	Several times	At least once a day	Several times a day
2. In the past week, did you have a sense of urgency to move your bowels?				
Never	Once or twice	Several times	At least once a day	Several times a day
3. In the past week, did you have pain or tenderness when you moved your bowels?				
Never	Once or twice	Several times	At least once a day	Several times a day
4. In the past week, did you have bleeding with your bowel movements?				
Never	Once or twice	Several times	At least once a day	Several times a day
5. In the past week, did you have abdominal cramping or pain?				
Never	Once or twice	Several times	At least once a day	Several times a day
6. In the past week, have you passed mucus from your rectum?				
Never	Once or twice	Several times	At least once a day	Several times a day
7. In the past week, did you feel the urge to move your bowels but have nothing to pass?				
Never	Once or twice	Several times	At least once a day	Several times a day

of toxicity rather than patient self-reported symptoms. Evidence suggests that there can be significant discrepancy between patient and physician assessment of the severity of symptoms [9]. To minimize this discrepancy, studies of quality-of-life changes ideally should be performed using validated patient self-assessment questionnaires or interviews. This study was undertaken to compare the self-reported gastrointestinal (GI) toxicities in men who receive neoadjuvant hormone therapy with their 3D-CRT and those who do not.

2. Materials and methods

2.1. Subjects and data collection

The initial study population consisted of 373 men who underwent consultation for prostate cancer treatment at the Mount Auburn Hospital in Cambridge, Massachusetts, between 1998 and 2001. Patients who underwent brachytherapy, radical prostatectomy, or postoperative radiation therapy were excluded. The first 40 patients who received androgen suppression therapy with their radiation and who had complete questionnaires, and the first 40 who received only conformal radiotherapy and who had complete questionnaires were included in the final analysis.

All 80 study patients had biopsy-proven adenocarcinoma of the prostate and had not received prior definitive cancer treatment. Disease-specific information such as pretreatment prostate-specific antigen (PSA) values, biopsy Gleason scores, and 1992 American Joint Committee on Cancer [10] clinical T-categories were recorded. In those patients who received neoadjuvant hormone therapy, the date of the first hormone injection was recorded, but the duration and timing of hormone therapy was left to the discretion of the clinician. Patients received monthly goserelin injections as their hormone therapy without bicalutamide or flutamide. Because all patients were treated at one institution, the treatment of radiation-related GI toxicity was generally consistent, and included dietary modification and antidiarrheal medication.

2.2. Patient self-assessment tool

Data on GI symptoms were collected using a previously validated self-administered questionnaire [11]. Patients were prospectively given the self-administered questionnaire before radiation treatment and at each subsequent weekly on-treatment visit. No patient received a monetary reward for completing the quality-of-life tool. Patients were asked to grade the frequency of symptoms during the past week according to a 5-point scale. Higher numbers indicated more frequent symptoms. Seven questions related to bowel function, specifically diarrhea, urgency, rectal pain, bleeding, abdominal cramping, mucus production, and tenesmus. The actual questions from the questionnaire are shown in Table 1.

2.3. Radiation planning and treatment techniques

All patients received 3D-CRT uniformly according to the Joint Center for Radiation Therapy standards from that time. Patients received a prescribed dose of 66.6 Gy, normalized to the 95% isodose curve, and a delivered dose of approximately 70 Gy in 1.8 Gy daily fractions. Computerized tomography-based simulation was used in the radiation planning of all patients. Neither rectal contrast nor urethrogram were used to mark the apex of the prostate during radiation planning.

The majority of treatment plans were designed to treat the prostate and seminal vesicles in a large field followed by a cone-down to the prostate only. Patients with advanced disease received full dose to both the prostate and seminal vesicles. The treatment volumes typically included the prostate with a 15-mm margin, delivered via a highly conformal, 4-field box technique. The total delivered dose, date of treatment planning, and treatment start date were recorded