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Treatment results of brachytherapy vs. external beam radiation therapy for intermediate-risk prostate cancer with 10-year followup

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ABSTRACT

PURPOSE: To compare 10-year treatment outcomes of brachytherapy vs. external beam radiation therapy for patients with intermediate-risk prostate cancer (IRPC).

METHODS AND MATERIALS: Between 2004 and 2007, 93 IRPC patients underwent brachytherapy using iodine-125 to a dose of 145 Gy without supplemental external radiation. A retrospective comparison was performed to a contemporary cohort of 597 patients treated with external beam radiation therapy to a median dose of 75.3 Gy using a propensity score-matched analysis.

RESULTS: Median followup was 7.8 years. With brachytherapy, 51.6% had Gleason score 7 vs. 72.0% for external radiation ($p < 0.001$). Median initial prostate-specific antigen was 8.3 for brachytherapy vs. 9.4 for external radiation ($p = 0.01$). Neoadjuvant androgen deprivation therapy was given in 59.5% of external radiation vs. 10.8% of brachytherapy patients ($p < 0.001$). The 10-year freedom from biochemical failure (FFBF) for brachytherapy was 81.7% vs. 54.5% for external radiation ($p = 0.002$). Unfavorable intermediate-risk patients experienced borderline significant improved FFBF with brachytherapy ($p = 0.08$). The 10-year freedom from salvage therapy for brachytherapy was 93.2% vs. 72.2% for external radiation ($p = 0.006$). There were no significant differences in distant metastases-free survival, prostate cancer-specific survival, or overall survival after adjusting for age. Multivariate analysis with propensity score matching showed that brachytherapy remained an independent predictor for improved FFBF ($p = 0.007$). Grade 1 and 2 late rectal complication rate was 6.5% for brachytherapy vs. 15.2% for external radiation ($p = 0.02$).

CONCLUSIONS: Brachytherapy using iodine-125 without supplemental external radiation is a reasonable treatment option for selected IRPC patients.

Keywords: Brachytherapy; Radiation therapy; Prostate cancer; Intermediate risk

Introduction

Prostate brachytherapy delivering high doses of radiation using ultrasound-guided placement of radioactive seeds has excellent 10-year outcomes (1–3). However, the vast majority of patients treated with brachytherapy were low-risk prostate cancer, in which there is no clear benefit to local treatment according to the Prostate Intervention vs.

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Observation Trial, yet local therapy did reduce all-cause mortality by 12.6% for intermediate-risk prostate cancer (IRPC) patients (4). The National Comprehensive Cancer Network (NCCN) guidelines recommend local treatment for patients with IRPC. Randomized studies of IRPC patients comparing external beam radiation therapy (EBRT) vs. brachytherapy without supplemental external radiation have not been performed. Our objective was to perform a retrospective comparison of IRPC patients treated with brachytherapy vs. EBRT with longer followup and a larger number of IRPC patients compared with prior studies (5, 6), while using the current Phoenix definition of biochemical failure (7). A propensity score-matched analysis was performed to minimize bias between treatment groups.

Methods and materials

Patient selection, staging, and work-up

This study included all IRPC patients who were treated with either brachytherapy or EBRT at our integrated, multifacility health care system between January 1, 2004 and December 31, 2007, but patients who received supplemental external radiation combined with brachytherapy were excluded from the study. A total of 93 patients underwent brachytherapy and were retrospectively compared to a contemporary cohort of 597 patients treated with EBRT. Clinical staging included a history and digital rectal examination using clinical T-stage from the 2002 American Joint Committee on Cancer staging system (8). Additional studies included initial prostate-specific antigen (iPSA), defined as the PSA ng/mL just before treatment, and transrectal ultrasound-guided needle sextant biopsies of the prostate with Gleason score (GS) histologic grading. IRPC was defined as one or more of the following prognostic factors: clinical stage of T2b, GS of 3 + 4 or 4 + 3, or iPSA of 10.1−20.0 (5). Percentage positive biopsy cores (PPBC) > 50% was calculated based on the pathology report. PPBC >50% was defined as more than 50% of the number of core biopsies containing adenocarcinoma of the total number cores taken. Favorable IRPC was defined as patients with only one intermediate-risk factor. Patients with multiple intermediate-risk factors, which also included PPBC >50%, or any patient with GS 4 + 3 were considered unfavorable (9). Charlson comorbidity index was used to assess overall health status between the treatment groups.

Treatment

For brachytherapy preplanning, a volumetric study was performed using transrectal ultrasound and placement of a Foley catheter to define the prostate and urethra. Using 0.4 mCi iodine-125 radioactive seeds, a minimum peripheral dose of 145 Gy was prescribed with a modified peripheral loading technique (10, 11), with a planning target volume (PTV) margin of 3−5 mm anterior, lateral, posterior-lateral, superior, 5−10 mm inferior but 0 mm PTV posterior-central. Our goal was to limit the urethral dose to less than 150% of the prescribed dose, and the goal for the rectum was to limit the volume that receives more than 100% of the prescribed dose to less than 1 cc. Postimplant dosimetry was performed on all patients using a CT scan of the pelvis 1−2 weeks after brachytherapy, fusing the preimplant volumetric ultrasound to the postimplant CT, using the VariSeed 8.0.1 fusion software to improve accuracy of our postimplant dosimetry. Percent volume that received ≥100% of the prescribed dose (V_{100}) and percentage of the prescribed dose delivered to 90% of the prostate (D_{90}) were calculated for the prostate. EBRT patients were treated using 3-dimensional conformal therapy techniques with 15 megavoltage photons using a 6-field approach, with 0.8-cm PTV margin around the prostate and seminal vesicles but 0.6-cm PTV posteriorly, but image guidance was not performed in our department from 2003 to 2007. The median dose prescribed to the isocenter was 75.3 Gy over eight and half weeks given 5 days per week. Overall, 94% of the patients undergoing EBRT received 75.3 Gy at the isocenter (range 73.5 Gy to 77.1 Gy). Neoadjuvant androgen deprivation therapy (NADT) was given in the form of Leuprolide, initiated 2−4 months before local therapy, and given during local therapy. NADT was given in 59.5% of the patients undergoing EBRT vs. 10.8% for brachytherapy ($p < 0.0001$). Neoadjuvant therapy was given a median of 4 months for brachytherapy patients vs. 6 months for the EBRT patients (Table 1).

Followup

Time zero was the date of brachytherapy or day 1 of EBRT treatment. Freedom from biochemical failure (FFBF) was defined based on the Phoenix definition of biochemical failure of PSA nadir + 2 ng/mL threshold (7). If the PSA rose 2 points above the nadir, followed by a decline in PSA below the nadir + 2 threshold, these were not counted as biochemical failure. Patients were instructed to followup every 6 months for 5 years, and annually thereafter, but since this was a retrospective study, followup was variable. Complications were graded using the Radiation Therapy Oncology Group grading system for late effects (12).

Statistical analysis

Patient characteristics were described with percentages for categorical factors, while median and range were used for continuous factors. Fisher's exact chi-square test was used to assess differences in categorical patient characteristics and complication rates between treatment modalities, while the Wilcoxon rank-sum test was used to assess differences in continuous factors between treatment groups. Kaplan−Meier estimates were calculated at 5 and 10 years,