ORIGINAL RESEARCH

Effect of Treatment Duration on Outcome after Radiotherapy for Prostate Cancer

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ABSTRACT

Aim: The aim of this study is to evaluate whether the duration of external beam radiotherapy (RT) influences treatment outcomes in prostate cancer patients. **Materials and methods:** 80 men with prostate cancer were treated with definitive radiotherapy (RT). Some intermediate- and high-risk patients did not receive androgen deprivation therapy due to physician or patient preference and timing related to clinical trial publications. Treatment interruptions were measured using the nontreatment day ratio (NTDR). Follow-up evaluations were based on prior institutional treatment protocols. Data analysis was done using SSPS software.Data analysis was done using SSPS software.Cox proportional hazards regression analysis was used for univariate and multivariate analyses. **Results:** A total of 80 patients were included in the study, with a median age of 55 years. The Gleason score distribution showed that 70% of patients had scores between 2–6, 20% had a score of 7, and 10% had scores between 8–10. Pretreatment PSA levels had a median value of 8.6 ng/mL, with 65% of patients having PSA ≤10 ng/mL, 20% having PSA between >10–19.99 ng/mL, and 15% having PSA ≥20 ng/mL. Regarding tumor stage, 57.5% of patients were classified as T1, 22.5% as T2, and 20% as T3. Risk stratification revealed that 52.5% of patients were in the low-risk category, 15% in the intermediate-risk category, and 32.5% in the high-risk group. **Conclusion:** Longer treatment duration was found to negatively impact low-risk patients.

Keywords: prostate, cancer, radiotherapy

INTRODUCTION

The use of external beam radiation therapy in the primary management of prostate cancer has recently come under sharp criticism. This has taken two forms. Primarily, its efficacy has been challenged by studies using new, objective, and exacting biochemical criteria of failure. A number of reports now attest to high rates of failure not only for the T3-4Nx group, but for Tl-2Nx men as well. Second, it has been argued that not only are the majority of patients not cured, but they are actually worse off than if they had been left untreated. [1-3]The probability of extraprostatic disease may be estimated based on clinical T-stage, pretreatment prostatic-specific antigen, Gleason score, and percent positive core biopsies. Patients with disease confined to the prostate may be treated with either prostatectomy or radiotherapy (RT). Patients with extraprostatic disease without evidence of distant metastases are best managed with RT. RT consisting of either external beam and/or brachytherapy results in a relatively high likelihood of cure, particularly for those with low- and intermediate-risk disease. The impact of elective nodal RT on survival is unclear. Dose escalation results in improved biochemical relapse-free survival compared with standard dose RT. Androgen deprivation therapy likely improves the probability of disease control in patients with high-risk cancers.[4-6]Hence; the present study was conducted for evaluating whether the duration of external beam radiotherapy (RT) influences treatment outcomes in prostate cancer patients.

MATERIALS AND METHODS

80 men with prostate cancer were treated with definitive radiotherapy (RT). The study used three-dimensional conformal RT (3D-CRT) and intensity-modulated RT (IMRT). Some intermediate- and high-risk patients did not receive androgen deprivation therapy due to physician or patient preference and timing related to clinical trial publications. Treatment interruptions were measured using the nontreatment day ratio (NTDR). Follow-up evaluations were based on prior institutional treatment protocols. Data analysis was done using SSPS software.Cox proportional hazards regression analysis was used for univariate and multivariate analyses.

RESULTS

Table 1: Patient characteristics

Characteristics	Value
Total patients	80
Age (years)	
Median	55
Range	20-60
Gleason Score	
2-6	56(70%)
7	16(20%)
8-10	8(10%)
Pretreatment PSA (ng/mL)	
Median	8.6
Range	0.5-136
≤10 ng/mL	52(65%)
>10–19.99 ng/mL	16(20%)
≥20 ng/mL	12(15%)
T Stage	
T1	46(57.5)
T2	18(22.5%)
T3	16 (20%)
Risk groups	
Low	42(52.5%)
Intermediate	12(15%)
High	26(32.5%)

A total of 80 patients were included in the study, with a median age of 55 years (range: 20–60). The Gleason score distribution showed that 70% of patients had scores between 2–6, 20% had a score of 7, and 10% had scores between 8–10. Pretreatment PSA levels had a median value of 8.6 ng/mL (range: 0.5–136 ng/mL), with 65% of patients having PSA ≤10 ng/mL, 20% having PSA between >10–19.99 ng/mL, and 15% having PSA ≥20 ng/mL.

Regarding tumor stage, 57.5% of patients were classified as T1, 22.5% as T2, and 20% as T3. Risk stratification revealed that 52.5% of patients were in the low-risk category, 15% in the intermediate-risk category, and 32.5% in the high-risk group.

Table 2: Cox proportional multivariate analyses for biochemical failure

Variable	Baseline	Hazard Ratio	P-value
All patients (n=80)			
NTDR	<30%	1.0	0.05
Gleason score	≤7	1.9	<0.002
T stage	T1-T2	2.1	<0.002
Pre treatment PSA	<20 ng/mL	3.0	<0.002
Radiation dose (Gy)	lower	1.1	0.20
Low risk (n=42)			
NTDR	<30%	1.5	0.04
Gleason score	**≤7**	1.0	0.04
T stage	T1-T2	1.9	0.02
Pre treatment PSA	<20 ng/mL	1.0	<0.021
Radiation dose (Gy)	lower	1.1	0.21
Intermediate risk (n=12)			
NTDR	<30%	1.0	0.21
Gleason score	**≤7**	1.2	0.03
T stage	T1-T2	1.1	0.23
Pre treatment PSA	<20 ng/mL	1.5	0.11
Radiation dose (Gy)	lower	1.1	0.12
High Risk (n=26)			
NTDR	<30%	1.7	0.34
Gleason score	**≤7**	2.2	0.31
T stage	T1-T2	1.3	0.23

Pre treatment PSA	<20 ng/mL	1.2	0.12
Radiation dose (Gy)	lower	1.1	0.12

DISCUSSION

External beam radiotherapy (RT) has been used as a curative treatment of prostate cancer for more than 5 decades, with the "modern" era emerging more than 3 decades ago. Its history is marked by gradual improvements punctuated by several quantum leaps that are increasingly driven by advancements in the computer and imaging sciences and by its integration with complementary forms of treatment. Consequently, the contemporary use of external beam RT barely resembles its earliest form, and this must be appreciated in the context of current patient care. The influence of predictive factors on the use and outcomes of external beam RT is presented, as is a selected review of the methods and outcomes of external beam RT as a single therapeutic intervention, in association with androgen suppression, or as a postoperative adjunct. Thus, the "state of the (radiotherapeutic) art" is presented to enhance the understanding of this treatment approach with the hope that this information will serve as a useful resource to physicians as they care for patients with prostate cancer.[6- 9]Hence; the present study was conducted for evaluating whether the duration of external beam radiotherapy (RT) influences treatment outcomes in prostate cancer patients.

ZietmanAL,et al assessed the long-term outcome of conventional external beam radiation therapy in the management of clinically confined prostate cancer and to examine the proposition that radiation accelerates tumor growth in those who fail treatment. One thousand and forty-four men with T1-4NxM0 prostate cancer treated by conventional external beam radiation therapy. At 10 years only 40% of the T1-2 group remained disease free. When subdivided by grade, the well-differentiated tumors (Gleason 1-2) exhibited a 53% actuarial 10-year disease-free survival, moderately differentiated (Gleason 3) 42%, and poorly differentiated (Gleason 4-5) 20%. The corresponding values for the T3-4 men were 33% for Gleason 1-2, 20% for Gleason 3, and 10% for Gleason 4-5. Overall the value for T3-4 tumors was 18% at 10 years. On relapse the median PSA doubling times for the T1-2 patients were predicted by histology: 18.8 months for Gleason 1-2 patients; 11.1 months for Gleason 3; and 9.6 months for Gleason 5. Significant differences were found between the Gleason 3 and the Gleason 4-5 groups ($p = 0.04$) and the Gleason 1-2 and the Gleason 4-5 groups ($p = 0.03$). A wide range of doubling times was seen within each grade group. When compared with recently reported data on selected T1-2 patients who were managed by expectant observation there was no advantage over the first decade (and certainly no disadvantage) in terms of metastasis-free survival or disease-specific survival for the irradiated Gleason 1-3 patients. However, a gain was seen for those with Gleason 4-5 tumors.Less than half of the T1-2NxM0 and less than one-fifth of the T3-4NxM0 patients receiving conventional radiation therapy were biochemically disease free at 10 years.[10]

Zhou EH, et al investigated the association of overall and disease specific survival with the 5 standard treatment modalities for prostate cancer (CaP): radical prostatectomy (RP), brachytherapy (BT), external beam radiation therapy (EBRT), androgen deprivation therapy (ADT), and no treatment (NT) within 6 months after CaP diagnosis. The study population included 10,179 men 65 years and older with incident CaP diagnosed between 1999 and 2001. Using the linked Ohio Cancer Incidence Surveillance System, Medicare, and death certificate files, we analyzed overall and disease specific survival through 2005 among the five clinically accepted therapies. Disease specific survival rates were 92.3% and 23.9% for patients with localized versus those with distant disease at 7 years, respectively. Controlling for age, race, comorbidities, stage, and Gleason score, results from the Cox multiple regression models indicated that the risk of CaP specific death was significantly reduced in patients receiving RP or BT, compared with NT. For localized disease, compared with NT, in mono-therapy cohort, RP and BT were associated with reduced hazard ratios (HR) =0.25 and 0.45 (95% confidence interval [0.13-0.48] and [0.23-0.87], respectively); while in the combination therapy cohort, HR were 0.40 [0.17-0.94] and 0.46 [0.27-0.80], respectively. The population-based study indicates that RP and BT are associated with improved survival outcomes.[11]

CONCLUSION

Longer treatment duration was found to negatively impact low-risk patients.

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