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BRACHYTHERAPY

Brachytherapy 16 (2017) 1106–1112

Prostate

Pretreatment 3T multiparametric MRI staging predicts for biochemical failure in high-risk prostate cancer treated with combination high-dose-rate brachytherapy and external beam radiotherapy

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ABSTRACT

PURPOSE: To determine whether pretreatment 3T multiparametric MRI (mpMRI) staging impacts biochemical recurrence-free survival (BRFS) or distant metastasis-free survival (DMFS) for men with high-risk prostate cancer treated with combination high-dose-rate (HDR) brachytherapy and external beam radiation therapy (EBRT).

MATERIALS AND METHODS: This institutional review board–approved retrospective study included a cohort of 37 men with high-risk prostate cancer treated with HDR brachytherapy and EBRT after 3T mpMRI. Kaplan–Meier analysis was used to evaluate whether mpMRI evidence of extracapsular extension or seminal vesicle invasion (SVI) resulted in differences in BRFS or DMFS. Pretreatment and treatment-related variables were evaluated for association with biochemical failure (Phoenix definition) and distant metastatic failure using univariate Cox regression analysis.

RESULTS: The median prostate-specific antigen at diagnosis was 9 ng/mL (range 2–100). Biopsy Gleason score (bGS) was ≤8 in 38% and nine in 62%. Clinical T-category was T1-T2 in 89%, T3a in 8%, and T3b in 3%. With a median followup of 30.6 months, actuarial 3-year BRFS and DMFS were 76% and 86%, respectively. Kaplan-Meier analysis revealed that mpMRI evidence of extracapsular extension or SVI resulted in significantly higher rates of both biochemical recurrence and distant failure. Using Cox regression analysis, only mpMRI evidence of SVI vs. no SVI predicted for biochemical failure (hazard ratio 13.98, $p = 0.0055$).

CONCLUSIONS: For high-risk prostate cancer treated with combination HDR brachytherapy and EBRT, mpMRI evidence of SVI predicted for biochemical failure, whereas traditional pretreatment variables did not. Therefore, pretreatment 3T mpMRI appears useful for identifying men who may benefit from treatment intensification.

Keywords: HDR brachytherapy; External beam radiotherapy; High-risk prostate cancer; Multiparametric MRI; Biochemical recurrence; Distant metastasis

Introduction

D'Amico *et al.* proposed a classification system to estimate the risk of biochemical failure after definitive treatment for prostate cancer almost 20 years ago (1). For this risk stratification system, men are identified as having low-, intermediate-, or high-risk disease based on clinical T-category, prostate-specific antigen (PSA) level, and biopsy Gleason score (bGS). More recently, revision of this risk stratification model, incorporating

Received 5 June 2017; received in revised form 2 July 2017; accepted 13 July 2017.

Financial disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest: None.

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1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2017.07.008

both percent positive biopsies and the number of National Comprehensive Care Network (NCCN) risk factors, has been proposed (2). The inclusion of these additional variables reflects that clinical T-category and bGS have variable accuracy for assessing prostate cancer tumor volume and pathologic Gleason score and highlights the need for improved prognostic information.

Aside from established risk factors, multiparametric MRI (mpMRI) at 3 Tesla (3T) field strength has emerged as an important pretreatment tool for predicting foci of clinically significant prostate cancer, pathologic Gleason score, pathologic stage, tumor multifocality, and tumor involvement of the neurovascular bundle (3–10). Multiparametric MRI-targeted biopsy can also more accurately ascertain the pathologic Gleason score (11–19). Pretreatment risk stratification changes are relatively common with the incorporation of mpMRI and mpMRI-targeted biopsies, occurring in approximately 20–40% of men undergoing these studies (20–22).

However, whether this risk migration based on 3T mpMRI stage and targeted bGS is inappropriate risk inflation or is more accurately identifying a high-risk cohort which would benefit from intensified treatment is not known. A previous study reported that pretreatment MRI staging independently predicts for biochemical recurrence in men treated with combined external beam radiation therapy (EBRT) and brachytherapy (23). However, this study evaluated a mixed cohort of both intermediate- and high-risk men treated before the use of 3T multiparametric imaging. Therefore, in this study we sought to evaluate whether pretreatment 3T mpMRI staging information predicts for biochemical recurrence or distant failure in men with NCCN-classified high-risk prostate cancer treated with combination high-dose-rate (HDR) brachytherapy and EBRT.

Methods and materials

Patient characteristics

This was an Institutional Review Board–approved, retrospective observational cohort study of 37 men with nonmetastatic, NCCN-classified high-risk prostate cancer consecutively treated with combined HDR brachytherapy and EBRT from 2010 to 2015 at a single, high-volume tertiary care institution. All men had at least one NCCN-classified high-risk feature (clinical T-category by digital rectal examination $\geq$ T3a, PSA $>$ 20 ng/mL, or bGS $\geq$ 8). All men had a technetium-99 bone scan to evaluate for metastatic disease. All men had a pelvic 3T mpMRI for locoregional staging. Most of the cohort (86%) had computed tomography (CT) of the abdomen and pelvis for locoregional staging preceding MRI as well, although in five men MRI was the only locoregional staging study. 3T mpMRI was performed with the following sequences: axial and coronal turbo spin-echo T2, calculated axial high b value diffusion-weighted (b value 1400 s/mm^2), and dynamic contrast-enhanced sequences after injection of 0.1 mmol/mg of intravenous gadolinium. An endorectal coil was used in 32% of the cohort (N = 12). MRI characteristics of the patient cohort were recorded from the clinical MRI reports.

Treatment characteristics

Treatment-related characteristics are presented in Table 1. Men were treated with intensity-modulated EBRT to the prostate and pelvic lymph nodes to a median dose of 45 Gy (range 39.6–50.4) in 1.8–2.0 Gy/Fx. An HDR brachytherapy boost was administered either prior to or following EBRT to a median dose of 21.75 Gy (range 15–24) in three fractions. The proximal seminal vesicles were always implanted during HDR brachytherapy, and the entire involved seminal vesicle was included if involved, based on MRI. CT-based treatment planning was performed for all patients. MRI was used to assist with contouring the anatomic boundaries of the prostate. However, MRI fusion was not performed. In addition, men also had gold fiducial markers placed in the prostate, which aided with anatomic delineation. All men were recommended to receive androgen deprivation therapy (ADT) but only 81% received it (median duration of 12 months [range 2–27]). The total duration of ADT was determined through

Table 1
Characteristics of the study cohort

Characteristic	Value
Age, years median (range)	68 (51–83)
PSA, ng/ml median (range)	9.3 (1.6–99.7)
Clinical T-Category (%)	
T1c	16 (43)
T2a	9 (24)
T2b	5 (14)
T2c	3 (8)
T3a	3 (8)
T3b	1 (3)
Biopsy Gleason score (%)	
4 + 3	1 (3)
4 + 4	8 (22)
3 + 5	5 (14)
4 + 5	19 (51)
5 + 4	4 (11)
Percent positive biopsies, % median (range)	46 (8–100)
External beam radiotherapy dose, Gy median (range)	45 (39.6–50.4)
Number of fractions, median (range)	25 (22–28)
High-dose rate brachytherapy dose, Gy median (range)	21.75 (15–24)
Number of fractions, median (range)	3 (1–4)
Androgen deprivation therapy use (%)	
No	7 (19)
Yes	30 (81)
Duration of androgen deprivation therapy use, months median (range)	11.7 (2.4–27.0)
Followup since completion of treatment, months median (range)	30.6 (7.2–62.8)