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Original Article

Pretreatment multiparametric MRI is independently associated with biochemical outcome in men treated with radiation therapy for prostate cancer

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Abstract

Purpose: The purpose of this study was to investigate the utility of pre-treatment multiparametric magnetic resonance imaging (mpMRI) in a modern cohort of intermediate and high-risk prostate cancer patients treated with primary radiotherapy.

Methods and materials: One hundred twenty three men with National Comprehensive Cancer Network (NCCN) intermediate or high-risk prostate cancer were treated with primary EBRT and/or brachytherapy and had evaluable pre-treatment mpMRI with endorectal coil. Images were assessed for the presence of radiographic extraprostatic extension (rEPE), seminal vesicle invasion (rSVI), lymph node involvement (LNI), sextant involvement, and largest axial tumor diameter. Imaging characteristics were analyzed along with clinical risk factors against freedom from biochemical failure (FFBF). Median follow-up time was 50 months.

Results: Fourteen (11%) men developed biochemical failure. The 5-year FFBF was 94% in intermediate-risk patients and 82% in high-risk patients ($p < 0.01$). mpMRI findings including rEPE (29% vs. 66%, $p < 0.01$), rSVI (6% vs. 25%, $p < 0.01$), LNI (1% vs. 30%, $p < 0.01$), and largest axial tumor size> 15 mm (27% vs. 48%, $p = 0.02$) were identified in men with intermediate vs. high risk prostate cancer, respectively. mpMRI features associated with 5-y FFBF biochemical failure on univariate analysis included rEPE (80% vs 98%), rSVI (55% vs. 96%), LNI (65% vs. 93%), and largest axial tumor size >15 mm (81% vs. 94%, all $p < 0.01$). Men without any high risk MRI finding had a 5-y FFBF of 100% vs. 81% ($p < 0.01$). Adverse imaging features (HR 8.9, $p < 0.01$) were independently associated with biochemical failure in a bivariate model analyzed alongside clinical risk category (HR 3.2, $p = 0.04$).

Conclusions: Pre-treatment mpMRI findings are strongly associated with biochemical outcomes in a modern cohort of intermediate and high-risk patients treated with primary radiotherapy. mpMRI may aid risk stratification beyond clinical risk factors in men treated with radiation therapy; further study is warranted to better understand how mpMRI can be used to individualize therapy.

Keywords: Prostate cancer; Multiparametric magnetic resonance imaging; Radiation therapy

1. Introduction

Risk-stratification for localized prostate cancer remains challenging, in part due to the heterogeneous nature of the disease [1]. Determining the optimal treatment course for an individual patient requires accurate staging and appropriate risk-stratification to balance treatment efficacy with unwanted side effects. Traditional clinical risk features such as Gleason score, prostate-specific antigen (PSA) level, and clinical stage aid in this process, however significant variability in prognosis remains. Furthermore, conventional imaging modalities such as ultrasound and computed tomography have inherent limitations in staging accuracy.

Multiparametric magnetic resonance imaging (mpMRI) is an advanced imaging modality with improved staging

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accuracy and the potential to improve risk stratification for localized prostate cancer. mpMRI combines anatomic and functional imaging features, with superior soft-tissue delineation as compared to CT [2,3]. mpMRI may also help identify areas of clinically significant disease and predict tumor aggressiveness [4], as supported by whole mount pathology studies correlating the site of relapse after definitive radiotherapy to the primary tumor focus [5]. The enhanced anatomic and functional information provided by mpMRI could impact radiation treatment planning decisions and potentially identify patients at increased risk of treatment failure [6]. This knowledge may be particularly important for patients receiving primary radiotherapy, as prostate biopsy alone may misclassify risk category compared to surgical staging. Furthermore, there is a desire to optimize cure with primary therapy since salvage local therapy after radiotherapy presents more potential risk for toxicity. mpMRI is increasingly utilized for work-up of localized prostate cancer, and has established applications for initial diagnosis, staging and surgical planning [7]. However, less is known about its utility and prognostic value in men treated with primary radiotherapy. We sought to investigate the prognostic value of pretreatment endorectal mpMRI in addition to commonly accepted clinical risk factors in a modern cohort of intermediate and high-risk prostate cancer patients treated with primary radiotherapy. We hypothesized that adverse imaging features on pretreatment mpMRI would be associated with biochemical failure, and that mpMRI could help tailor therapy for men who undergo radiation therapy to the prostate.

2. Methods and materials

Using a prospectively maintained institutional database, we retrospectively identified 257 men with National Comprehensive Cancer Network (NCCN) intermediate or high-risk localized prostate cancer treated with primary external beam radiation therapy (EBRT) and/or brachytherapy between 2006 and 2013 [8]. Patient demographics, treatment information, and follow-up information were prospectively recorded. Review of patient outcomes was conducted with approval from our institutional review board.

Patient characteristics are summarized in Table 1. In 138 (54%) patients, pretreatment mpMRI was obtained. risk category was determined based on clinical stage, and mpMRI results did not formally change a patient's clinical risk classification. mpMRI was available over the time period of study and ordered at the discretion of treating physician. mpMRI was routinely ordered after consultation in radiation oncology for men undergoing active surveillance or brachy therapymonotherapy, and to provide further risk-stratification when additional information was desirable to inform treatment decisions for men who were candidates for EBRT. Fifteen patients with mpMRIs were

Table 1
Patient characteristics (n = 257)

	Number (percentage) or median (range)			
Characteristic	Overall (n = 257)	MRI (n = 123)	No MRI (n = 134)	*P*−value
Age, years	68 (47−88)	67 (47−88)	69 (50−88)	0.029
Pretreatment PSA, ng/ml	9.71 (1.1−165)	9.2 (1.9−109.1)	10 (1.1−165)	0.048
NCCN risk group				
Intermediate	150 (58%)	79 (64%)	71 (53%)	0.068
High	107 (42%)	44 (36%)	63 (47%)	
Clinical T−stage				
T1c−T2a	165 (64%)	80 (65%)	85 (63%)	0.968
T2b−T2c	45 (17.5%)	22 (18%)	23	
T3	45 (17.5%)	20 (16%)	25	
Unknown	2 (1%)	1 (1%)	1	
Gleason score				
6	22 (8.5%)	9 (7%)	13 (10%)	0.275
7	160 (62%)	84 (68%)	76 (56%)	
8	40 (15.5%)	17 (14%)	23 (17%)	
9	35 (14%)	13 (11%)	22 (17%)	
Treatment				
EBRT	224 (87%)	96 (78%)	126 (94%)	0.001
Brachytherapy	30 (12%)	25 (20%)	7 (5%)	
EBRT + brachytherapy	3 (1%)	2 (2%)	1 (1%)	
Radiation Dose, Gy				
EBRT	78 (75.6−79.2)	78 (75.6−79.2)	78 (75.6−79.2)	
Brachytherapy	145 (144−145)	145 (144−145)	145 (144−145)	
Androgen deprivation therapy	144 (56%)	64 (52%)	80 (60%)	0.216
Yes				

PSA = prostate-specific antigen; NCCN= national comprehensive cancer network; EBRT= external beam radiation therapy.