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Impact of multiparametric magnetic resonance imaging on risk group assessment of patients with prostate cancer addressed to external beam radiation therapy

Serena Pullini[a], Marco Andrea Signor[b], Martina Pancot[a], Chiara Zuiani[a], Massimo Bazzocchi[a], Sandro Fongione[b], Rossano Girometti[a,*]

[a] Institute of Diagnostic Radiology, Department of Medical and Biological Sciences, University of Udine, Azienda Ospedaliero-Universitaria Santa Maria della Misericordia, via Colugna, 50-33100 Udine, Italy
[b] Department of Oncological Radiation Therapy, Azienda Ospedaliero-Universitaria Santa Maria della Misericordia, Piazzale S. M. della Misericordia, 15-33100 Udine, Italy

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ABSTRACT

Purpose: To investigate the impact of multiparametric magnetic resonance imaging (mpMRI) on risk group assessment of patients with prostate cancer (PCa) initially addressed to external beam radiation therapy (EBRT).
Materials and methods: We prospectively performed mpMRI (3.0Tsystem) in 44 patients addressed to EBRT, using a multiparametric protocol (high-resolution multiplanar T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging). Risk group was assessed in accordance with the National comprehensive cancer network (NCCN) categories, by combining prostate-specific-antigen level, Gleason score and the T-stage as established by digital rectal examination (clinical risk assessment; c-RA) versus mpMRI (mpMRI-risk assessment; mpMRI-RA). The agreement between c-RA and mpMRI-RA was investigated using Cohen's kappa.
Results: Patients were included in very low/low risk, intermediate risk, high risk, very high risk and metastatic NCCN categories in 10 (22.7%), 18 (40.9%), 15 (34.1%), 1 (2.3%) and 0 cases using c-RA vs. 8 (18.2%), 14 (31.8%), 14 (31.8%), 4 (9.1%) and 4 (9.1%) cases using mpMRI-RA, respectively, with only moderate agreement ($k = 0.43$). mpMRI-RA determined risk downgrading in 2/44 patients (4.5%), and risk upgrading in 16/44 patients (36.3%). After mpMRI, EBRT remained indicated in all patients.
Conclusion: mpMRI changed clinical risk stratification in about 41% of patients with PCa, with potential impact on EBRT planning.

1. Introduction

Prostate cancer (PCa) is one of the most common malignancies in elderly men, as well as the second leading cause of cancer-related death in males [1]. Prevalence increases with age: almost 34% of men over the age of 50 and up to 70% aged 80 years or older have histological evidence of PCa [2]. However, most patients with a diagnosis of PCa die with the disease, rather than of the disease, suggesting significant overdiagnosis and overtreatment underlying current management options [3]. Differentiating between life-threatening versus not significant PCa at the moment of diagnosis is still challenging.

On this basis, several risk-group classifications have been defined in order to assess the risk of local recurrence and metastatic disease [4–7], including those produced by the Ameri-

Abbreviations: Pca, prostate cancer; mpMRI, multiparametric magnetic resonance imaging; EBRT, external beam radiation therapy; DRE, digital rectal examination; TRUS, transrectal ultrasonography; PSA, prostate-specific antigen; GS, Gleason score; NCCN, National comprehensive cancer network; DWI, diffusion-weighted Imaging; DCE, dynamic contrast-enhanced Imaging; c-RA, clinical risk assessment; mpMRI-RA, mpMRI-based risk assessment; PI-RADS, Prostate imaging reporting and data system; ESUR, European society of urogenital radiology; TNM, tumour node metastasis; SPAIR, spectrally adiabatic inversion recovery; ECE, extra-capsular extension; SVI, seminal vesicles invasion; ADT, androgen deprivation therapy.

* Corresponding author at: Institute of Diagnostic Radiology, Department of Medical and Biological Sciences, University of Udine, Azienda Ospedaliero-Universitaria Santa Maria della Misericordia, via Colugna, 50-33100 Udine, Italy.
E-mail addresses: serepul@libero.it (S. Pullini), signor.marco@aoud.sanita.fvg.it (M. Signor), martypancot@libero.it (M. Pancot), zuiani.chiara@aoud.sanita.fvg.it (C. Zuiani), bazzocchi.massimo@aoud.sanita.fvg.it (M. Bazzocchi), fongione.sandro@aoud.sanita.fvg.it (S. Fongione), rgirometti@sirm.org (R. Girometti).

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Table 1
Risk-group assessment with associated treatment options, according to NCCN criteria [8].

Risk group		Description	Treatment option (initial therapy)	
Clinically localized	Very low	• T1c • GS ≤6 • PSA <10 ng/mL • PSA density <0.15 ng/mL/g • Fewer than 3 prostate biopsy cores positive; ≤50% cancer in each core	LE ≥ 20 years	• AS • EBRT or BRACHYTX • RP ± PLND[b]
			LE 10–20 years	AS
			LE < 10 years	Observation
	Low	• T1-T2a • GS ≤6 • PSA <10 ng/mL	LE ≥ 10 years	• AS • EBRT or BRACHYTX • RP ± PLND[b]
			LE < 10 years	Observation
	Intermediate[a]	• T2b-T2c or • GS = 7 or • PSA = 10–20 ng/mL	LE ≥ 10 years[b]	• RP ± PLND[c] • EBRT ± ADT (4–6 mo) ± BRACHYTX • BRACHYTX ALONE
			LE < 10 years	• EBRT ± ADT (4–6 mo) ± BRACHYTX • BRACHYTX Alone • Observation
	High[a]	• T3a or • GS = 8–10 or • PSA > 20 ng/mL		• EBRT + ADT (2–3 years) • EBRT + BRACHYTX ± ADT (2–3 years) • RP + PLND
Locally advanced	Very high	• T3b-T4 • Primary Gleason pattern = 5 or • >4 cores with GS 8–10		• EBRT + ADT (2-3 years) • EBRT + BRACHYTX ± ADT (2–3 years) • RP + PLND (in select patients: with no fixation) • ADT (in select patients[d])
	Metastatic	• Any T, N1		• ADT • EBRT + ADT (2–3 years)
		• Any T, Any N, M1		• ADT

T1c, T2a–b–c, T3a–b, T4 T-stage, based on TNM system [18]; GS = Gleason score; PSA = prostate specific antigen; LE = life expectancy; AS = active surveillance; EBRT = external beam radiation therapy; BRACHYTX = brachytherapy; RP = radical prostatectomy; PLND = pelvic lymph node dissection; ADT = androgen deprivation therapy.
[a] Patients with multiple adverse factors may be shifted into the next highest risk group.
[b] Active surveillance of intermediate and high-risk clinically localized cancers is not recommended in patients with a life expectancy > 10 years.
[c] If predicted probability of lymph node metastasis ≥2%.
[d] Primary therapy with ADT should be considered only for patients who are not candidates for definitive therapy.

can National comprehensive cancer network (NCCN) [8], which are of widespread use and the reference for treatment choice in our radiation therapy department. Risk assessment has a pivotal role in planning a cost-effective treatment tailored to cancer aggressiveness and patients' status and expectations [9]. In most systems, including the NCCN one, risk assessment is performed by combining clinical T-stage as assessed by digital rectal examination (DRE), prostate-specific antigen (PSA) level and the Gleason score (GS) found at histopathological examination after biopsy [4–8].

Multiparametric magnetic resonance imaging (mpMRI) provides T2-weighted high-resolution images of the prostate, coupled with functional information from diffusion-weighted Imaging (DWI) and dynamic contrast-enhanced imaging (DCE). Based on this "all-in-one" approach, mpMRI is a useful tool for cancer staging [10,11] and has an ever-increasing role in the detection of clinically significant PCas in several clinical scenarios [12]. To our knowledge, though many previous studies investigated the impact of mpMRI in staging cancer in patients belonging to different risk groups [10,13], little is known about the role of mpMRI as an independent tool to provide risk stratification, i.e. in defining risk categories themselves [14]. We hypothesized that, since mpMRI is more objective and reproducible [15,16], it might replace DRE in assessing the T-stage, which in turn might be used to refine risk stratification. This would be of particular interest in patients addressed to external beam radiation therapy (EBRT), in whom pathological T-stage is unavailable by definition. As a consequence, cancer T-stage and risk stratification should be assessed as more reliably as possible before treatment planning.

On this basis, we aimed to investigate the impact of mpMRI-based T staging on risk group assessment of patients addressed to EBRT. In particular, we evaluated the agreement between clinical risk assessment (c-RA; DRE + PSA level + GS) vs. mpMRI-based risk assessment (mpMRI-RA; mpMRI + PSA level + GS).

2. Materials and methods

2.1. Study population

This study is compliant with laws and regulations of our country, and was performed as a branch of an institutional review board-approved trial investigating the impact of 3.0T mpMRI on the management of prostate cancer. Participants expressed informed consent.

Between March 2013 and March 2015, we prospectively performed mpMRI for local staging of biopsy-proven prostate cancer in all patients addressed to EBRT by referring radiotherapists. Indi-