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Association Between Prostate Imaging Reporting and Data System (PI-RADS) Score for the Index Lesion and Multifocal, Clinically Significant Prostate Cancer

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Abstract

Background: The ability to identify clinically significant prostate cancer (csPCa) has dramatically improved with the introduction of multiparametric magnetic resonance imaging (mpMRI). Given the growing interest in targeted biopsy and focal therapy, improving our knowledge on the relationship between mpMRI parameters and the ability to predict csPCa multifocality is mandatory.
Objective: To assess whether the Prostate Imaging Reporting and Data System (PI-RADS) score for the index lesion (IL) may predict multifocal csPCa undetected by mpMRI.
Design, setting, and participants: The study included 343 patients who underwent mpMRI of the prostate with subsequent biopsy between 2014 and 2017 at a single tertiary care referral centre.
Intervention: Lesions with a PI-RADS v.2 score $\geq$2 detected at mpMRI (IL) were targeted with a fusion biopsy (Bx) approach (mpMRI-Bx). Moreover, each patient underwent a random extended transrectal ultrasound-guided biopsy (TRUS-Bx) during the same session.
Outcome measurements and statistical analysis: csPCa outside the IL was defined as disease detected at TRUS-Bx with a Gleason score (GS) $\geq$ 3 + 4 and equal to or greater than the GS for the IL. The extent of csPCa detected in target and random cores was reported and stratified according to the GS and PI-RADS score for the IL. The probability of diagnosing csPCa outside the IL according to the PI-RADS score was also assessed in multivariable logistic regression analyses (MVA) after accounting for confounders.
Results and limitations: The detection rate for csPCa outside the IL was 30%. The detection rate for csPCa at TRUS-Bx was 8% for PI-RADS 2, 15% for PI-RADS 3, 36% for PI-RADS 4, and 58% for PI-RADS 5 lesions (p = 0.03). Overall, the median length of

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csPCa found at TRUS-Bx and thus missed at mpMRI was 2.6 mm. However, the length significantly increased with PI-RADS score for the IL, and was 1.8, 2.3, 2.8, and 3.8 mm for PI-RADS 2, 3, 4, and 5 lesions, respectively ($p = 0.03$). On MVA, PI-RADS 4 (odds ratio [OR] 7.6; $p = 0.008$) and PI-RADS 5 scores (OR 17.3; $p < 0.001$) were independent predictors of the presence of csPCa outside the IL. The study is limited by its retrospective design.

Conclusions: Overall, the accuracy of mpMRI in identifying multifocal csPCa is poor, missing low-volume csPCa in approximately 30% of patients. Moreover, the rate and the extent of csPCa undetected by mpMRI significantly increased with the PI-RADS score for the IL, which can thus be considered a proxy for tumour multifocality.

Patient summary: The accuracy of multiparametric magnetic resonance imaging in identifying prostate cancer multifocality is poor. False negative findings were highly related to the PI-RADS score of the index lesion. These findings raise concerns about the indication for targeting the index lesion only when considering prostate biopsy and focal approaches.

1. Introduction

The widespread use of prostate-specific antigen (PSA) has led to an increase in the diagnosis of localised, low-risk prostate cancer (PCa) [1–3]. In order to reduce such overdiagnosis, novel diagnostic and therapeutic approaches have been developed. Multiparametric magnetic resonance imaging (mpMRI) of the prostate has demonstrated high diagnostic accuracy for clinically significant PCa (csPCa) [4]. For this reason, mpMRI has been included in targeted biopsy strategies, and can increase the detection of csPCa while reducing the rates of insignificant disease relative to systematic transrectal ultrasound-guided biopsy (TRUS-Bx) [5]. Although current guidelines support the use of concurrent systematic biopsy at the time of targeted biopsy, some authors still consider targeted biopsy alone sufficient for the detection of csPCa [6]. Moreover, mpMRI of the prostate is also mandatory for accurate selection of PCa patients who may be candidates for focal therapy. In this context, general consensus has been reached in treating only the mpMRI-detected index lesion (IL) in men suitable for focal therapy [7,8]. The rationale for targeting the IL only with biopsy and focal approaches is the concept that the IL is the driver of prognosis in the majority of PCa patients [9]. However, no prospective study has ever fully confirmed this hypothesis. This issue is key, since other high-grade non-ILs potentially missed by mpMRI may themselves represent a source of systemic dissemination if left untreated using focal approaches. Although previous studies have assessed the risk of csPCa outside the IL, data on the association between IL features and multifocal aggressive PCa are currently scarce [10,11]. Such risk-assessment would be key for proper risk stratification and selection of candidates for focal therapy given the possible non-negligible risk of harbouring csPCa outside the IL, even if smaller in size. We hypothesised that the IL characteristics, in terms of the Prostate Imaging Reporting and Data System (PI-RADS) score, are strictly related to the presence of csPCa outside the IL. Specifically, we hypothesised that higher PI-RADS scores for the IL are associated with a higher probability of harbouring multifocal significant disease. To address this issue, we used data for a contemporary cohort of patients who underwent mpMRI and subsequent mpMRI-Bx in association with TRUS-Bx.

2. Patients and methods

2.1. Study population

The study cohort consisted of 343 consecutive patients who underwent mpMRI of the prostate with subsequent transrectal targeted fusion mpMRI-Bx and concomitant TRUS-Bx at a single tertiary care referral centre between January 2013 and February 2017. Data were prospectively collected from the first case performed.

2.2. mpMRI

All patients underwent a 1.5-T mpMRI study (Achieva and Achieva dStream, Philips Medical Systems, Best, Netherlands) with a phased-array surface coil and an endorectal coil (BPX-15; Bayer Medical Care, Indianola, PA, USA). According to the European Society of Urogenital Radiology guidelines, the imaging protocol consisted of multiplanar T2-weighted images, diffusion-weighted imaging (DWI, with *b* values of 0–800–1400/1600 s/mm^2; apparent diffusion coefficient maps were automatically elaborated), dynamic contrast-enhanced (DCE) MRI, and delayed T1-weighted images with fat suppression. For patients who had previously received one or more sets of biopsies, all mpMRI scans were performed at least 4 wk after prostate biopsy, and precontrast T1-weighted images were recorded to rule out post-biopsy haemorrhagic artefacts. The mpMRI images were scored and reported according to PI-RADS v.2 [12]. Three experienced radiologists analysed the mpMRI findings. Imaged lesions with a PI-RADS v.2 score $\geq$2 detected at mpMRI were targeted. Moreover, all patients regardless of PI-RADS score underwent random biopsy during the same session.

2.3. Prostate biopsy technique and histopathologic examination

A software registration fusion approach was used to biopsy the lesions visualised on mpMRI. In the case of multiple suspicious lesions detected at mpMRI, each lesion was targeted. Each patient also concomitantly underwent a standard 12-core random systematic biopsy (TRUS-Bx)