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Combined Clinical Parameters and Multiparametric Magnetic Resonance Imaging for Advanced Risk Modeling of Prostate Cancer—Patient-tailored Risk Stratification Can Reduce Unnecessary Biopsies

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Abstract

Background: Multiparametric magnetic resonance imaging (mpMRI) is gaining widespread acceptance in prostate cancer (PC) diagnosis and improves significant PC (sPC; Gleason score $\geq 3+4$) detection. Decision making based on European Randomised Study of Screening for PC (ERSPC) risk-calculator (RC) parameters may overcome prostate-specific antigen (PSA) limitations.
Objective: We added pre-biopsy mpMRI to ERSPC-RC parameters and developed risk models (RMs) to predict individual sPC risk for biopsy-naïve men and men after previous biopsy.
Design, setting, and participants: We retrospectively analyzed clinical parameters of 1159 men who underwent mpMRI prior to MRI/transrectal ultrasound fusion biopsy between 2012 and 2015.
Outcome measurements and statistical analysis: Multivariate regression analyses were used to determine significant sPC predictors for RM development. The prediction performance was compared with ERSPC-RCs, RCs refitted on our cohort, Prostate Imaging Reporting and Data System (PI-RADS) v1.0, and ERSPC-RC plus PI-RADSv1.0 using receiver-operating characteristics (ROCs). Discrimination and calibration of the RM, as well as net decision and reduction curve analyses were evaluated based on resampling methods.

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Results and limitations: PSA, prostate volume, digital-rectal examination, and PI-RADS were significant sPC predictors and included in the RMs together with age. The ROC area under the curve of the RM for biopsy-naïve men was comparable with ERSPC-RC3 plus PI-RADSv1.0 (0.83 vs 0.84) but larger compared with ERSPC-RC3 (0.81), refitted RC3 (0.80), and PI-RADS (0.76). For postbiopsy men, the novel RM's discrimination (0.81) was higher, compared with PI-RADS (0.78), ERSPC-RC4 (0.66), refitted RC4 (0.76), and ERSPC-RC4 plus PI-RADSv1.0 (0.78). Both RM benefits exceeded those of ERSPC-RCs and PI-RADS in the decision regarding which patient to receive biopsy and enabled the highest reduction rate of unnecessary biopsies. Limitations include a monocentric design and a lack of PI-RADSv2.0.
Conclusions: The novel RMs, incorporating clinical parameters and PI-RADS, performed significantly better compared with RMs without PI-RADS and provided measurable benefit in making the decision to biopsy men at a suspicion of PC. For biopsy-naïve patients, both our RM and ERSPC-RC3 plus PI-RADSv1.0 exceeded the prediction performance compared with clinical parameters alone.
Patient summary: Combined risk models including clinical and imaging parameters predict clinically relevant prostate cancer significantly better than clinical risk calculators and multiparametric magnetic resonance imaging alone. The risk models demonstrate a benefit in making a decision about which patient needs a biopsy and concurrently help avoid unnecessary biopsies.

1. Introduction

Prostate-specific antigen (PSA) screening leads to increased prostate cancer (PC) detection and a shift from advanced to earlier disease stages [1,2]. However, PSA testing lacks specificity, resulting in unnecessary biopsies [3]. Simultaneously, random transrectal ultrasound (TRUS)-guided biopsy suffers from poor sampling, leading to underdetection of PC in approximately 50% of cases compared with radical prostatectomy (RP) specimen and transperineal mapping biopsy [4,5]. Currently, the most promising candidate to overcome these limitations is multiparametric magnetic resonance imaging (mpMRI) using a standardized reporting system (Prostate Imaging Reporting and Data System [PI-RADS]) [6,7]. Compared with RP specimens, mpMRI detects 85–95% of index lesions and significant PC (sPC) [8,9]. Fusion-targeted biopsies (FTBs) of suspicious mpMRI lesions improve the detection of sPC by 30% [10].

To identify men with sPC and concurrently to avoid unnecessary biopsies, multivariable risk-based approaches have been introduced [2,3,11]. Using risk calculators (RCs) built on European Randomized Study of Screening for PC (ERSPC) data, Roobol et al demonstrated that 33% of standard biopsies can be avoided in men who are at risk of PC below 12.5% [3]. However, recent RCs do not include mpMRI data. FTB of mpMRI-suspicious lesions alone is a promising strategy to reduce overdetection of insignificant disease, but MRI-invisible sPC is overlooked by such an approach [10,12–14]. Here, we added prebiopsy mpMRI to clinical parameters and developed risk models (RMs) to determine individual sPC risk using a validated biopsy approach combining FTBs and transperineal systematic saturation biopsies (SBs) as reference [8].

2. Patients and methods

2.1. Study population

Consecutive patients were enrolled and registered into a prospective database assessing MRI-targeted/TRUS fusion biopsy between 2012 and 2015. Institutional review board approval was obtained (S011/2011), and all participants provided written informed consent. Subgroups were reported previously [8,15].

The study population consisted of 1159 retrospectively analyzed patients. Inclusion criteria were mpMRI with PI-RADS scoring and fusion biopsy at our department. In total, the sample consists of 670 (58%) biopsy-naïve men and 489 (42%) men with previous TRUS biopsy. A total of 129 men under active surveillance and 15 men who had missing data were excluded (Supplementary Fig. 1). For 660 biopsy-naïve men and 355 men with previous TRUS biopsy, full data on PI-RADS, biopsy-outcome, PSA, age, digital-rectal examination (DRE), prostate volume (PV), prior biopsy, lesions on TRUS, and ERSPC-RCs were available. Those samples served for RM development, internal validation, and comparisons with ERSPC-RCs, PI-RADSv1.0, and combined ERSPC-RCs and PI-RADSv1.0.

2.2. Imaging

All mpMRI examinations were performed using a 3 T system (Magnetom; Siemens, Erlangen, Germany) using a multichannel-body-surface coil (Supplementary Table 1). All image analyses were prospectively performed according to PI-RADSv1.0 by or under the supervision of expert uroradiologists (H.P.S., D.B., and M.C.R., with 7–12 yr experience in prostate MRI) [6]. Overall, PI-RADS scores for each lesion were determined on a five-point Likert scale and entailed assignment of a separate score for each of the T2-weighted, DW, and dynamic contrast-enhanced imaging sequences [6]. PV was calculated on T2-weighted images (www.itksnap.org).

2.3. Biopsy protocol

All men underwent transperineal FTB with rigid software registration using BiopSee (MedCom, Darmstadt, Germany) of MRI-suspicious lesions first (2–5 cores, median 2 per lesion) and then SB adjusted to PV (median 24 cores), as previously described [8,15]. Transperineal grid-directed biopsy performed under general anesthesia is our standard technique, the sPC-detection accuracy of which has been validated using RP specimens [8].

2.4. Histopathology

Histopathological analyses were performed under the supervision of a uropathologist (W.R.) specialized in prostate assessment according to International Society of Urological Pathology standards. sPC was defined as Gleason score (GS) $\geq$ 3 + 4.

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