Risk Stratification of Equivocal Lesions on Multiparametric Magnetic Resonance Imaging of the Prostate

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Purpose: We systematically analyzed the records of patients with PI-RADS™ (Prostate Imaging Reporting and Data System) 3 lesions, which are called equivocal according to PI-RADS version 2, using prostate multiparametric magnetic resonance imaging and magnetic resonance imaging targeted biopsies. Systematic transrectal ultrasound guided biopsies served as the reference standard.

Materials and Methods: A total of 120 consecutive patients were retrospectively included in the study. In these patients the overall PI-RADS score was 3 after 3 Tesla T2-weighted imaging, diffusion weighted imaging and dynamic contrast enhanced multiparametric magnetic resonance imaging as well as subsequent targeted magnetic resonance imaging/ultrasound fusion guided biopsies plus systematic 12-core transrectal ultrasound guided biopsies. The study end points were the prostate cancer detection rate, the Gleason score distribution, the prostate cancer location and risk stratification by subgroup analyses.

Results: Prostate cancer was detected in 13 of 118 patients for a detection rate of 11%, including 5 patients (4.2%) with a Gleason score of $3 + 4 = 7$ or greater. Three of the 212 lesions (1.4%) in the transition zone and 6 of the 64 (9.4%) in the peripheral zone were positive for prostate cancer. Multiparametric magnetic resonance imaging revealed patterns of peripheral prostatitis combined with diffuse stromal hyperplasia in 54% of the patients with prostate cancer. Prostate volume was significantly lower in patients with prostate cancer ($p = 0.015$) but differences in prostate specific antigen levels were not statistically significant ($p = 0.87$). Prostate specific antigen density was higher in patients with prostate cancer (0.19 vs 0.12 ng/ml/ml).

Conclusions: Low grade prostate cancer (Gleason score $3 + 3 = 6$) can develop in patients with an overall PI-RADS score of 3. Prostate cancer with a Gleason score of $3 + 4 = 7$ or greater can be detected by multiparametric magnetic resonance imaging with a high degree of certainty. Gleason score $4 + 3 = 7$ or greater prostate cancer is unlikely in PI-RADS 3 lesions. Therefore, these patients should primarily undergo followup multiparametric magnetic resonance imaging. In patients with a combination of multiparametric magnetic resonance imaging aspects of extensive prostatitis and diffuse stromal hyperplasia low prostate volume and/or high prostate specific antigen density biopsy might be considered.

Key Words: prostatic neoplasms, image-guided biopsy, magnetic resonance imaging, ultrasonography, diagnostic imaging

Abbreviations and Acronyms

AS = anterior stroma
FUS-GB = MRI/ultrasound fusion guided biopsy
GS = Gleason score
mp-MRI = multiparametric MRI
MRI = magnetic resonance imaging
PCa = prostate cancer
PI-RADS™ = Prostate Imaging Reporting and Data System
PSA = prostate specific antigen
PSAD = PSA density
PZ = peripheral zone
SB = systematic biopsy
TB = targeted biopsy
TRUS = transrectal ultrasound
TRUS-GB = TRUS guided biopsy
TZ = transition zone

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MULTIPARAMETRIC MRI of the prostate is increasingly becoming routine in various aspects of PCa management.[1] PSA screening followed by systematic TRUS biopsy has led to a strong increase in the detection of PCa at early stages. However, this goes along with a risk of over diagnosis and overtreatment since most detected tumors are low risk cancers that are unlikely to clinically manifest.[2–4] Especially among urologists there is still disagreement on whether these low risk cancers need to be detected or should rather remain unnoted to prevent overtreatment. Moreover, an inappropriate high number of biopsies is not only inconvenient and alarming for our patients but they also carry a risk of potential complications.[5,6]

A well-known limitation of TRUS biopsies is limited sensitivity for anteriorly located tumors.[7] Furthermore, systematic TRUS guided biopsies often underestimate the final Gleason grade of the tumor compared with histology after radical prostatectomy, potentially hindering patients from receiving adequate therapeutic options.[8] Prostate mp-MRI prior to a potential biopsy can help prevent unnecessary biopsies and potential complications. On the other hand, targeted biopsies after initial negative TRUS biopsy can detect clinically significant PCa if highly suspicious lesions are found on mp-MRI.[7,9] To strengthen clinical confidence in this technique prostate MRI must provide similarly reliable results internationally.

The PI-RADS version 2 guidelines represent an important milestone in standardizing prostate MRI interpretation by providing a precise system to assess the different pulse sequences.[10] Also, the entire MRI examination can be classified according to the risk of clinically significant PCa (PI-RADS score 1 to 5). By following these instructions a considerable number of patients receive a PI-RADS score of 3, which is termed equivocal according to PI-RADS. The diagnostic and therapeutic consequences in these cases remain unclear since the reported prevalence of prostate cancer in biopsied PI-RADS 3 lesions varies widely in the current literature.[11–14] However, the protocols of these studies are inconsistent. Protocols have not been standardized due to different biopsy techniques and reference standards, different or modified PI-RADS versions, or varying mp-MRI acquisition combined with a wide range of experience and quality.

Proposals have been made to further adjust the current PI-RADS scoring system to improve the discriminatory power of mp-MRI.[15] However, to our knowledge there has been no agreement to date on whether patients with a PI-RADS overall score of 3 can be safely treated with followup MRI or need immediate biopsy, especially if they already have undergone a previous negative biopsy.

Therefore, we evaluated the risk of PCa in patients with an overall PI-RADS version 2 score of 3 on standardized, qualitative mp-MRI and clinical conditions that might be associated with higher risk to improve the treatment of this patient population.

MATERIAL AND METHODS

Study Design

A total of 120 consecutive patients with an overall PI-RADS version 2 score of 3 and subsequent targeted FUS-GB plus systematic 12-core TRUS-GB between October 2013 and March 2017 were retrospectively included in this study. None of the patients were diagnosed with PCa prior to MRI. The indications for biopsy or rebiopsy were elevated PSA and/or suspicious digital rectal examination, or another clinical suspicion for PCa. The study was approved by the local ethics committee with a waiver of written informed consent. The end points were 1) PCa detection rate, 2) GS distribution, 3) location of PCa lesions, 4) detection rates of TRUS-GB and FUS-GB, and 5) risk stratification by subgroup analyses.

Imaging

Multiparametric MRI was performed on a 3 Tesla Magnetom Trio™ MRI scanner with a body coil in accordance with the recommendations of a European consensus meeting. The detailed imaging parameters were published previously, including T2-weighted TSE sequences in 3 planes (axial voxel size $0.5 \times 0.5 \times 3.0$ mm and field of view 130 mm), echoplanar imaging diffusion-weighted imaging (voxel size $1.5 \times 1.5 \times 3.0$ mm, b-values 0, 500 and 1,000 s/mm^2 plus 1,400 s/mm^2 or greater) and dynamic contrast enhanced imaging (voxel size $1.5 \times 1.5 \times 3.0$ mm, scan time 3 minutes and temporal resolution less than 9 seconds).[16] Apparent diffusion coefficient parameter maps were calculated using the standard monoexponential model. MRI was interpreted by radiologists with 3 to 7 years of experience with reading prostate MRI according to PI-RADS versions 1 and 2. Prostate volume was measured on axial and sagittal T2-weighted images (height $\times$ width $\times$ depth/2). PSAD was calculated by dividing PSA blood levels by prostate volume.

Biopsy

Transrectal targeted FUS-GB (2 targeted cores per lesion) followed by blinded systematic 12-core TRUS-GB was done on a Urostation® device with an 18 gauge fully automatic biopsy gun (Bard Medical, Karlsruhe, Germany) in all cases. Since systematic TRUS-GB was performed by the same operator, blinding was guaranteed by a standardized biopsy plan that included lateral and mid lobar cores at the base, middle, and apex of each prostate lobe. Biopsies were performed by 2 urologists (CA and AH) with 8 and 7 years of experience, respectively, with MRI targeted transrectal prostate biopsy.

Data and Image Analysis

Demographic data, clinical data, MRI and biopsy data were reviewed and described according to START (Standards of Reporting for MRI-targeted Biopsy Studies).[17]