The Roles of Multiparametric Magnetic Resonance Imaging, PCA3 and Prostate Health Index—Which is the Best Predictor of Prostate Cancer after a Negative Biopsy?

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Abbreviations and Acronyms

bGS = biopsy Gleason score
DCA = decision curve analysis
DRE = digital rectal examination
DWI = diffusion weighted imaging
%fPSA = free PSA rate
mp-MRI = multiparametric magnetic resonance imaging
MRI = magnetic resonance imaging
PB = prostate biopsy
PCa = prostate cancer
PCA3 = prostate cancer antigen 3
PHI = Prostate Health Index
PSA = prostate specific antigen
RB = repeat biopsy
tPSA = total PSA

Purpose: In patients with a negative prostate biopsy and persistent suspicion of prostate cancer, additional analyses such as the PCA3 score, PHI and multiparametric magnetic resonance imaging have been proposed to reduce the number of unnecessary repeat biopsies. In this study we evaluate the diagnostic accuracy of PCA3, PHI, multiparametric magnetic resonance imaging and various combinations of these tests in the repeat biopsy setting.

Materials and Methods: A total of 170 patients with an initial negative prostate biopsy and persistent suspicion of prostate cancer were enrolled in this prospective study. The patients underwent measurements of the total prostate specific antigen and free prostate specific antigen rate, along with PHI, PCA3 tests and multiparametric magnetic resonance imaging before standard repeat biopsy that was performed by urologists blinded to the multiparametric magnetic resonance imaging results. Multivariate logistic regression models with various combinations of PCA3, PHI and multiparametric magnetic resonance imaging were used to identify the predictors of prostate cancer with repeat biopsy, and the performance of these models was compared using ROC curves, AUC analysis and decision curve analysis.

Results: In the ROC analysis the most significant contribution was provided by multiparametric magnetic resonance imaging (AUC 0.936), which was greater than the contribution of the PHI+PCA3 model ($p < 0.001$). In the multivariate logistic regression analysis only multiparametric magnetic resonance imaging was a significant independent predictor of prostate cancer diagnosis with repeat biopsy ($p < 0.001$). The results of the decision curve analysis confirmed that the most significant improvement in the net benefit was provided by multiparametric magnetic resonance imaging.

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Nothing to disclose.

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Editor's Note: This article is the second of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 286 and 287.

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Conclusions: Multiparametric magnetic resonance imaging provides high diagnostic accuracy in identifying patients with prostate cancer in the repeat biopsy setting compared with PCA3 and PHI.

Key Words: prostatic neoplasms; biopsy; magnetic resonance imaging; prostate cancer antigen 3, human

In cases of suspicion of prostate cancer, patients are currently subjected to prostate biopsy, which remains the gold standard for diagnosis.[1] This approach has its limits because in 25% to 30% of patients with PCa the neoplastic tissue is not included in the samples.[2] Moreover in patients with persistently increased PSA and negative PB, the repetition of biopsies does not increase the detection rate of PCa, which indeed decreases progressively.[3] Because of the additional number of samples there is a significant risk of complications (infection, bleeding, acute urinary retention), anxiety and social-sanitary costs.[4]

Recently various biomarkers have been studied to increase the ability to predict PCa diagnosis, especially in patients with persistent suspicion of cancer and a previous negative PB. The most promising biomarkers are PCA3 and [-2]proPSA (p2PSA), along with its derivative, the Prostate Health Index.[5–9] Other authors have emphasized the role of mp-MRI in PCa diagnosis, taking advantage of the anatomical, morphological and functional information that it provides.[10–15]

To evaluate the role of new biomarkers and mp-MRI in this setting we conducted a prospective observational study to evaluate the diagnostic accuracy of PCA3, PHI, mp-MRI and various combinations of the 3 tests in patients undergoing a standard repeat biopsy with an initial negative PB who maintained a high suspicion of harboring PCa.

MATERIALS AND METHODS

Study Design and Population

The study was performed between March 2011 and April 2013, after obtaining the approval of the ethics committee of our institution, San Luigi Hospital in Orbassano, Italy. Patients were prospectively included in the study if they had a negative initial PB (12 samples) and if they had a high suspicion of harboring PCa that warranted RB.

The inclusion criteria were persistently increased PSA and/or positive DRE. The exclusion criteria were contraindications for undergoing PB (ie cannot interrupt anticoagulant therapy) or mp-MRI (ie claustrophobia, presence of magnetically activated implanted devices, metallic implants in sensitive areas) or previous prostate treatment (ie transurethral prostate resection). Moreover patients suspected of having anteriorly located PCa on mp-MRI were noted by the radiologist and were excluded from the study.

Biomarkers

All patients underwent serum measurements of tPSA, %fPSA and PHI before repeat biopsy. The PHI analyses were performed using Hybritech Calibrated Access® assays (Beckman Coulter, Brea, California)[16] after processing with a Unicel® DxI 800 Immunoassay System analyzer (Beckman Coulter). All men underwent PCA3 testing before RB via a Progensa® PCA3 assay (Gen-Probe Inc, San Diego, California) according to the manufacturer's specific instructions.

Prostate mp-MRI

All patients underwent mp-MRI with a 1.5-T scanner (Signa Excite HD, GE Healthcare, Wauwatosa, Wisconsin) using a 4-channel phase array coil combined with an endorectal coil (Medrad, Warrendale, Pennsylvania). The prostate and seminal vesicle anatomy was assessed on T2-weighted images in the axial, coronal and sagittal planes. T1 fast spin echo axial images were generated to identify areas of intraprostatic hemorrhage and to evaluate the pelvic nodes and bones. Functional information was obtained by DWI and dynamic contrast enhanced MRI. DWI was performed using axial echo planar imaging sequences at different b-values. The sequence parameters satisfied the recommendations from a European consensus meeting that were published after the beginning of this study.[17] Further details on technical parameters are reported in the supplementary Appendix (http://jurology.com/).

All MR images were sent to a workstation and post-processed (Functool v. 9.4.05a, GE Healthcare). A single experienced radiologist analyzed the mp-MRI findings. The radiologist was blinded to the pathologist biopsy reports and to the biomarker results. For the purpose of this study the radiologist had to choose between suspicion of PCa (positive mp-MRI) or no suspicion of PCa (negative mp-MRI). The signs considered suspicious for PCa are reported in the supplementary Appendix.[10,14,18] Overall the mp-MRI finding was considered positive if at least 2 of the 3 MR sequences (T2-weighted, DWI and dynamic contrast enhanced MRI) produced suspicious findings.

Prostate Biopsy and Pathology

All patients then underwent RB under transrectal ultrasound guidance in an ambulatory setting. Biopsies were performed according to the Rodríguez-Covarrubias et al protocol using a Hawk Ultrasound scanner 2102 EXL with a biplanar transducer 8808 (B-K Medical, Herlev, Denmark) and a disposable core biopsy instrument (MaxCore®) with an 18G needle and 18 mm length of sample notch.[19] When the prostate volume was less than 60 cc the RB consisted of 18 needle biopsy cores, whereas when the prostate volume was 60 cc or greater a 24-sample biopsy scheme was adopted. Two dedicated urologists blinded to