The Efficacy of Multiparametric Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Risk Classification for Patients with Prostate Cancer on Active Surveillance

Pedro Recabal, Melissa Assel, Daniel D. Sjoberg, Daniel Lee, Vincent P. Laudone, Karim Touijer, James A. Eastham, Hebert A. Vargas, Jonathan Coleman and Behfar Ehdaie*

From the Urology Service, Sidney Kimmel Center for Prostate and Urologic Cancers (PR, VPL, KT, JAE, JC, BE), Department of Epidemiology and Biostatistics (MA, DDS, BE) and Department of Radiology (HAV), Memorial Sloan Kettering Cancer Center, Department of Urology, Weill-Cornell Medical College, New York Presbyterian Hospital (DL), New York, New York, and Urology Service, Fundacion Arturo Lopez Perez, Santiago, Chile (PR)

Abbreviations and Acronyms

AS = active surveillance
GU = genitourinary
mp = multiparametric
MRI = magnetic resonance imaging
ROI = regions of interest
TRUS = transrectal ultrasound

Purpose: We determined whether multiparametric magnetic resonance imaging targeted biopsies may replace systematic biopsies to detect higher grade prostate cancer (Gleason score 7 or greater) and whether biopsy may be avoided based on multiparametric magnetic resonance imaging among men with Gleason 3+3 prostate cancer on active surveillance.

Materials and Methods: We identified men with previously diagnosed Gleason score 3+3 prostate cancer on active surveillance who underwent multiparametric magnetic resonance imaging and a followup prostate biopsy. Suspicion for higher grade cancer was scored on a standardized 5-point scale. All patients underwent a systematic biopsy. Patients with multiparametric magnetic resonance imaging regions of interest also underwent magnetic resonance imaging targeted biopsy. The detection rate of higher grade cancer was estimated for different multiparametric magnetic resonance imaging scores with the 3 biopsy strategies of systematic, magnetic resonance imaging targeted and combined.

Results: Of 206 consecutive men on active surveillance 135 (66%) had a multiparametric magnetic resonance imaging region of interest. Overall, higher grade cancer was detected in 72 (35%) men. A higher multiparametric magnetic resonance imaging score was associated with an increased probability of detecting higher grade cancer (Wilcoxon-type trend test $p < 0.0001$). Magnetic resonance imaging targeted biopsy detected higher grade cancer in 23% of men.

Accepted for publication February 15, 2016.

All authors contributed equally to the study design, conduct of the study, data collection and analysis, and manuscript draft.

Supported by the Sidney Kimmel Center for Prostate and Urologic Cancers, NIH/NCI Cancer Center Support Grant P30 CA008748, and by David H. Koch through the Prostate Cancer Foundation.

The data used in this study were reviewed by the IRB and granted a Waiver of Authorization determined to be exempt from human subject research consent requirement.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

* Correspondence: Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 353 East 68th St., New York, New York 10065 (telephone: 646-422-4406; FAX: 212-988-0759; e-mail: ehdaieb@mskcc.org).

For another article on a related topic see page 562.

0022-5347/16/1962-0374/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2016.02.084
Vol. 196, 374-381, August 2016
Printed in U.S.A.

Magnetic resonance imaging targeted biopsy alone missed higher grade cancers in 17%, 12% and 10% of patients with multiparametric magnetic resonance imaging scores of 3, 4 and 5, respectively.

Conclusions: Magnetic resonance imaging targeted biopsies increased the detection of higher grade cancer among men on active surveillance compared to systematic biopsy alone. However, a clinically relevant proportion of higher grade cancer was detected using only systematic biopsy. Despite the improved detection of disease progression using magnetic resonance imaging targeted biopsy, systematic biopsy cannot be excluded as part of surveillance for men with low risk prostate cancer.

Key Words: prostatic neoplasms, watchful waiting, magnetic resonance imaging, image-guided biopsy

For men diagnosed with Gleason 3+3 prostate cancer, cancer specific mortality is low and active surveillance is widely recommended by clinical guidelines.[1] The AS strategy requires serial biopsies to detect possibly more aggressive tumors, defined by Gleason grade and tumor volume. Currently, systematic TRUS guided prostate biopsy is the standard technique, but it is limited due to its tendency to misclassify cancer risk as suggested by a significant rate of upgrading (23% to 61%) after radical prostatectomy in patients meeting different published criteria for AS who undergo surgery.[2,3] In a large prospective study of men on AS, routine systematic biopsies during followup detected progression to Gleason grade 3+4 or greater disease in only 9.5% after a median followup of 6.4 years.[4] Although the baseline risk among the groups was varied, the difference in rates of upgrading may suggest that some cases managed with AS may be misclassified and harbor higher risk disease.

The role of multiparametric MRI for prostate cancer detection has been evaluated in different clinical settings.[5–9] Recent studies suggest MRI targeted biopsy may be superior to systematic biopsy for risk classification.[10] We evaluate the efficacy of prostate MRI targeted biopsy to detect higher grade cancer (defined here as Gleason score 3+4 or greater) and describe the efficacy to rule out higher grade disease in patients on AS for Gleason 3+3 prostate cancer. In addition, we assess whether MRI targeted biopsies may be used instead of systematic biopsy or whether biopsy might be avoided based on the level of suspicion of detecting cancer on imaging depicted by MRI score.

METHODS AND MATERIALS

Patient Cohort

After institutional review board approval we reviewed our prospective clinical database of men with low risk prostate cancer on AS. We included men with previously confirmed clinically localized Gleason grade 3+3 prostate cancer enrolled on AS, who had mpMRI and a prostate biopsy performed between January 2014 and January 2015. All biopsies performed elsewhere were reread at our institution. Patients with a diagnosis of Gleason 3+4 or greater prostate cancer and those who received definitive treatment for prostate cancer were excluded from analysis. We identified 71 (34%) patients who had no ROI on mpMRI (mpMRI score less than 3) who underwent a systematic biopsy and 135 (66%) patients with at least 1 region of interest on mpMRI (mpMRI score of 3 to 5) who underwent MRI targeted biopsy of the ROI followed by a systematic biopsy of the remaining areas of the prostate. Median number of previous biopsies was 2. Our reporting is consistent with START (Standards of Reporting for MRI-targeted Biopsy Studies) guidelines.[10]

Imaging

Patients underwent mpMRI at least 3 months after the previous biopsy. Images were acquired under a magnetic field of 1.5 T (24, 12%) with endorectal coil or 3 T (182, 88%) without endorectal coil. Most of the studies were performed at our institution (184, 89%) and outside studies were reread at our institution. MRI systems (GE Healthcare, Wauwatosa, Wisconsin) and multichannel phased array coils were used. Sequences acquired included T1-weighted images, T2-weighted images, diffusion weighted sequences and parametric maps of apparent diffusion coefficients, and dynamic contrast enhanced sequences. A detailed description of the planes and acquisition parameters can be found in the supplementary Appendix (http://jurology.com/). MpMRIs were evaluated as per standard clinical care by 1 of 6 members of our institution's GU radiology section, with 6 to 15 years of experience in GU radiology.

MpMRIs were scored on a 5-point suspicion Likert scale as previously published.[11] This scale was developed at our institution using whole mount prostatectomy specimens as a reference. It has been used in multiple studies investigating the value of prostate mpMRI,[12–15] and appears to be equivalent[16–18] to the original version of the recently developed PI-RADS (Prostate Imaging Reporting and Data System),[19] which is an expert consensus statement and still undergoing wide validation. PI-RADS is not currently used at our institution and, therefore, was not evaluated in this study in which standard of care mpMRI interpretation was assessed. A shape was drawn by the radiologist on the T2-weighted images surrounding each region of interest where the interpreting radiologist's subjective degree of suspicion for the presence of cancer was at least 50% (eg mpMRI score 3 or greater) for subsequent MRI targeted biopsy.