Magnetic Resonance Imaging Targeted Biopsy Improves Selection of Patients Considered for Active Surveillance for Clinically Low Risk Prostate Cancer Based on Systematic Biopsies

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Abbreviations and Acronyms

ADC = apparent diffusion coefficient
AS = active surveillance
CCL = cancer core length
DRE = digital rectal examination
mp = multiparametric
MRI = magnetic resonance imaging
PCa = prostate cancer
PSA = prostate specific antigen
RP = radical prostatectomy
SB = systematic biopsy
TB = targeted biopsy
TRUS = transrectal ultrasound
TZ = transition zone

Accepted for publication February 26, 2015.
Study received institutional review board approval.

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Purpose: Current selection criteria for active surveillance based on systematic biopsy underestimate prostate cancer volume and grade. We investigated the role of additional magnetic resonance imaging targeted biopsy in reclassifying patients eligible for active surveillance based on systematic biopsy.

Materials and Methods: We performed a study at 2 institutions in a total of 281 men with increased prostate specific antigen. All men met certain criteria, including 1) prebiopsy magnetic resonance imaging, 12-core transrectal systematic biopsy and 2 additional magnetic resonance imaging targeted biopsies of lesions suspicious for cancer during the same sequence as systematic biopsy, and 2) eligibility for active surveillance based on systematic biopsy results. Criteria for active surveillance were prostate specific antigen less than 10 ng/ml, no Gleason grade 4/5, 5 mm or less involvement of any biopsy core and 2 or fewer positive systematic biopsy cores. Patient characteristics were compared between reclassified and nonreclassified groups based on magnetic resonance imaging targeted biopsy results.

Results: On magnetic resonance imaging 58% of the 281 patients had suspicious lesions. Magnetic resonance imaging targeted biopsy was positive for cancer in 81 of 163 patients (50%). Of 281 patients 28 (10%) were reclassified by magnetic resonance imaging targeted biopsy as ineligible for active surveillance based on Gleason score in 8, cancer length in 20 and Gleason score plus cancer length in 9. Suspicious areas on magnetic resonance imaging were in the anterior part of the prostate in 15 of the 28 men (54%). Reclassified patients had a smaller prostate volume (37 vs 52 cc) and were older (66.5 vs 63 years) than those who were not reclassified ($p < 0.05$).

Conclusions: Magnetic resonance imaging targeted biopsy reclassified 10% of patients who were eligible for active surveillance based on systematic biopsy. Its incorporation into the active surveillance eligibility criteria may decrease the risk of reclassification to higher stages during followup.

Key Words: prostatic neoplasms, magnetic resonance imaging, diagnostic imaging, biopsy, watchful waiting

0022-5347/15/1942-0350/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.02.2938
Vol. 194, 350-356, August 2015
Printed in U.S.A.

ACTIVE surveillance for low risk PCa may reduce the overtreatment of clinically insignificant PCa while retaining the option of definitive therapy in patients reclassified as higher risk during followup. AS selection criteria for low risk PCa using 12-core SB include fewer than 2 to 3 positive cores, Gleason score 6 or less and 3 to 5 mm maximum involvement of any core.[1,2] These criteria are associated with a risk of reclassification during followup in up to 30% of cases.[3] Upgrading rates up to 50% were reported when RP specimens were used as the reference test.[4] Therefore, there is a need for new diagnostic tools that might improve the estimation of tumor grade and extent, and the selection of patients for AS.

An immediate repeat biopsy series that was evaluated in several studies is part of some AS protocols.[5] mp-MRI is a powerful tool for identifying clinically significant PCa with 80% sensitivity for detecting index tumors[6] and 86% for detecting tumors greater than 0.5 cm^3, a volume considered clinically significant.[7] Haffner et al found that TB of suspicious areas detected on prebiopsy MRI showed higher detection accuracy for significant PCa than 12-core SB (0.98 vs 0.88, $p < 0.001$).[8] Cancers that are missed or under staged by SB are predominantly located in the anterior part of the prostate.[9] These anterior tumors are detected and better sampled by MRI-TB and account for 19% of cancers.[10]

MRI was recently proposed to help in the selection and monitoring of patients for AS.[11,12] However, studies are lacking of the role of prebiopsy MRI and TB at the time of selection for AS in patients presenting with suspected PCa referred for biopsy.[13] We investigated the role of MRI-TB in reclassifying patients eligible for AS based on SB.

MATERIALS AND METHODS

Study Design and Population

This multicenter study was performed at Lille University Hospital and Paris Pitié-Salpêtrière University Hospital. At each institution 300 to 400 prostate biopsies and 600 to 800 prostate MRIs are performed each year. We obtained institutional review board approval and study enrollment required us to provide study information and verbal patient consent. The study period extended from January 2008 to December 2012 at the Lille center and from October 2008 to December 2012 at the Paris center.

All consecutive patients were enrolled who presented with suspected PCa due to increased PSA and/or abnormal DRE, were referred for TRUS guided biopsies and underwent prebiopsy MRI (fig. 1). AS criteria were PSA less than 10 ng/ml, no Gleason grade 4 or 5, 5 mm or less (definition 1) or 3 mm or less (definition 2) involvement of any biopsy core and 2 or fewer positive SB cores. Cancer was reclassified based on MRI-TB when TB results were Gleason grade 4 or 5 (Gleason score 7 or greater), or greater than 5 mm or greater than 3 mm CCL based on any TB.

MRI Performance and Reporting

Imaging was performed using a 1.5 Tesla clinical system with a pelvic phased array coil. Examination included T2-weighted and diffusion-weighted imaging with an ADC map and dynamic contrast enhanced sequences. Dedicated uroradiologists with greater than 10 years of expertise with prostate imaging evaluated all images.[14] A 5-point Likert scale based on MRI findings was assigned to each abnormal lesion as previously described.[15] This was similar to the ESUR (European Society of Urogenital Radiology) scoring system, which was not available during the entire study period.[16] Criteria for the likelihood of malignancy were classified as nonsuspicious (score 1 or 2) or suspicious (score 3 or greater). Areas suspicious for cancer (score 3 or greater) were evaluated simultaneously by a radiologist and a urologist, and mapped with the standardized 27-section reporting scheme, which allowed the urologist performing the biopsies to target the suspicious area on TRUS.[17]

Biopsy Technique

Two TBs of MRI suspicious lesions were done immediately before SB using visual estimation during TRUS. The standardized MRI reporting scheme was used for lesions greater than 10 mm. For lesions less than 10 mm software based 3-dimensional TRUS/MRI fusion was performed with Urostation® or MyLab70™. Of the patients 53 in Lille and 25 in Paris were part of a previous study comparing 2 approaches to MRI-TB (visual estimation and software MRI-TRUS fusion) in which no difference was seen in cancer identification and sampling quality.[15] As a reference test all patients underwent 12-core TRUS guided SB, including 6 lateral and 6 mid lobar cores from the base, middle region and apex of the gland. SB tracks were not influenced by MRI findings. Adverse events and complications were recorded.

Surveillance Protocol

PSA was measured every 6 months during 2 years and annually thereafter in stable cases. Patients were offered DRE, mp-MRI and prostate biopsy 12 months after the entry biopsy.

Statistical Analysis

Data were analyzed with SPSS®, version 17.0. We used the Fisher exact test to compare binary variables and the Wilcoxon test to compare continuous variables.

RESULTS

Reclassification Rate and Adverse Effects

MRI revealed suspicious lesions in 163 of the 281 patients (58%) eligible for AS based on SB according to definition 1. TB performed in all 163 patients showed no cancer in 82 (50%) and cancer in 81 (50%). In the 81 patients with cancer on TB CCL was 5 mm or less and Gleason score was 6 in 53 (65%) (not reclassified) while CCL was greater than 5 mm and/or Gleason score was greater than 6 in 28 (35%). These 28 cases were reclassified due to Gleason grade 4/5 in 8 (29%), CCL greater than