Serial Magnetic Resonance Imaging in Active Surveillance of Prostate Cancer: Incremental Value

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Purpose: We assessed whether changes in serial multiparametric magnetic resonance imaging can help predict the pathological progression of prostate cancer in men on active surveillance.

Materials and Methods: A retrospective cohort study was conducted of 49 consecutive men with Gleason 6 prostate cancer who underwent multiparametric magnetic resonance imaging at baseline and again more than 6 months later, each followed by a targeted prostate biopsy, between January 2011 and May 2015. We evaluated whether progression on multiparametric magnetic resonance imaging (an increase in index lesion suspicion score, increase in index lesion volume or decrease in index lesion apparent diffusion coefficient) could predict pathological progression (Gleason 3 + 4 or greater on subsequent biopsy, in systematic or targeted cores). Diagnostic performance of multiparametric magnetic resonance imaging was determined with and without clinical data using a binary logistic regression model.

Results: The mean interval between baseline and followup multiparametric magnetic resonance imaging was 28.3 months (range 11 to 43). Pathological progression occurred in 19 patients (39%). The sensitivity, specificity, positive predictive value and negative predictive value of multiparametric magnetic resonance imaging was 37%, 90%, 69% and 70%, respectively. Area under the receiver operating characteristic curve was 0.63. A logistic regression model using clinical information (maximum cancer core length greater than 3 mm on baseline biopsy or a prostate specific antigen density greater than 0.15 ng/ml^2 at followup biopsy) had an AUC of 0.87 for predicting pathological progression. The addition of serial multiparametric magnetic resonance imaging data significantly improved the AUC to 0.91 (p=0.044).

Abbreviations and Acronyms

ADC = apparent diffusion coefficient

AS = active surveillance

MCCL = maximum cancer core length

mpMRI = multiparametric magnetic resonance imaging

MRI = magnetic resonance imaging

MR-US = magnetic resonance-ultrasound

NPV = negative predictive value

PCa = prostate cancer

PPV = positive predictive value

PSA = prostate specific antigen

PSAD = PSA density

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Conclusions: Serial multiparametric magnetic resonance imaging adds incremental value to prostate specific antigen density and baseline cancer core length for predicting Gleason 6 upgrading in men on active surveillance.

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

THE majority of prostate cancer currently presents as localized disease and nearly half of cases are characterized as low grade.[1] Thus, active surveillance has become an increasingly important management strategy, with the goal of avoiding unnecessary side effects associated with definitive therapy without missing the window for curative treatment, if necessary.

Serial prostate biopsy is a critical component of most contemporary AS regimens.[2] The current standard of care is systematic, extended, sextant, 12-core transrectal ultrasound guided biopsy (systematic biopsy) which does not target specific lesions and, therefore, may under sample clinically significant disease.[3] There is an unmet need for better noninvasive monitoring of men with PCa.

Multiparametric MRI provides a noninvasive means to assess the entire prostate gland from an anatomical and functional perspective. Findings on mpMRI are significant predictors of subsequent biopsy results.[4,5] Therefore, mpMRI may be a useful adjunct in the followup of men on AS through detecting disease progression and through directing subsequent targeted biopsy. The value of mpMRI in the initial selection of men for AS is well established but the usefulness of serial mpMRI in the followup of men on AS has not yet been confirmed.[6]

Before serial mpMRI can be incorporated into AS regimens in a meaningful way, the 2 key questions that must be addressed are what is the natural history of mpMRI index lesions over time and what mpMRI findings constitute disease progression?[7] Few studies to date have evaluated serial mpMRI findings in men with low risk PCa[8–12] and these questions remain largely unanswered. In this study we assessed whether changes in serial mpMRI can help predict the pathological progression of PCa in men on AS.

MATERIALS AND METHODS

Study Population

An institutional review board approved, HIPAA (Health Insurance Portability and Accountability Act) compliant review was performed on 1,048 consecutive men who underwent MR-US fusion guided prostate biopsy between January 2011 and May 2015. The current analysis is a retrospective review of a subset of these prospectively collected data. From this cohort 108 men with 2 or more mpMRI examinations at least 6 months apart, each followed by MR-US fusion biopsy, were identified. In men with more than 2 sets of serial mpMRI/MR-US fusion biopsy sessions, the first and last sets were selected. An additional 6 men were excluded from analysis due to nonroutine protocol on baseline or followup mpMRI, leaving 102 eligible men. Then 15 men were excluded due to Gleason 3 + 4 or greater on baseline MR-US fusion biopsy and 38 were excluded due to benign baseline biopsy, leaving a final cohort of 49 men with Gleason 6 PCa, who were enrolled in the UCLA AS program.[6] Patients had serum PSA measurement at each MR-US fusion biopsy. Prostate volume was calculated using manual contouring of mpMRI examinations (fig. 1).

MRI Technique

Multiparametric MRI examinations were performed on a 3.0 T Siemens platform (Siemens MAGNETOM, Trio, Verio, Skyra or Prisma, Siemens Medical Solutions, Malvern, Pennsylvania) without an endorectal coil. The protocol included T2-weighted imaging, diffusion weighted imaging and dynamic contrast enhanced imaging.

Image Analysis

Image analysis was performed by 2 fellowship trained genitourinary radiologists (DJM, SSR), both of whom have interpreted more than 1,000 prostate mpMRIs. Radiologists were blinded to clinicopathological findings at the initial image interpretation. Each lesion was assigned a suspicion score, ranging from 1 (normal) to 5 (highly suspicious for PCa), using a previously published standardized assessment system.[13]

A third radiologist with 1 year of experience in prostate mpMRI (ERF) reviewed all studies quantitatively, and recorded volume and mean ADC for each lesion. Data analysis was performed on a DynaCAD workstation (Invivo, Gainesville, Florida).

For each mpMRI examination the lesion with the highest overall suspicion score was selected as the index lesion. In cases where more than 1 lesion had the same suspicion score, the lesion with the lower mean ADC was selected as the index lesion, based on our previous work demonstrating that quantitative lesion ADC is an important predictor of Gleason score (fig. 2).[14]

MR-US Fusion Biopsy and Pathological Analysis

The reference standard in all cases was MR-US fusion biopsy using the Artemis device (Eigen, Grass Valley, California), which included systematic biopsy of 12 sites and additional targeted biopsy of any suspicious lesions identified on mpMRI.[15] One core of tissue was obtained approximately every 3 mm along the longest diameter of each target, ie for a 9 mm target, 3 cores would be obtained. For targets exceeding 15 mm, a maximum of