Pathological and 3 Tesla Volumetric Magnetic Resonance Imaging Predictors of Biochemical Recurrence after Robotic Assisted Radical Prostatectomy: Correlation with Whole Mount Histopathology

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Abbreviations and Acronyms

3D = 3-dimensional

3TmpMRI = 3 Tesla prostate mpMRI

ADC = apparent diffusion coefficient

BCR = biochemical recurrence

mpMRI = multiparametric MRI

MRI = magnetic resonance imaging

PCa = prostate cancer

PI-RADS® = Prostate Imaging-Reporting and Data System

PSA = prostate specific antigen

RALP = robotic assisted laparoscopic radical prostatectomy

T2W = T2-weighted imaging

v2 = version 2

WMHP = whole mount thin section histopathology

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Purpose: We sought to identify the clinical and magnetic resonance imaging variables predictive of biochemical recurrence after robotic assisted radical prostatectomy in patients who underwent multiparametric 3 Tesla prostate magnetic resonance imaging.

Materials and Methods: We performed an institutional review board approved, HIPAA (Health Insurance Portability and Accountability Act) compliant, single arm observational study of 3 Tesla multiparametric magnetic resonance imaging prior to robotic assisted radical prostatectomy from December 2009 to March 2016. Clinical, magnetic resonance imaging and pathological information, and clinical outcomes were compiled. Biochemical recurrence was defined as prostate specific antigen 0.2 ng/cc or greater. Univariate and multivariate regression analysis was performed.

Results: Biochemical recurrence had developed in 62 of the 255 men (24.3%) included in the study at a median followup of 23.5 months. Compared to the subcohort without biochemical recurrence the subcohort with biochemical recurrence had a greater proportion of patients with a high grade biopsy Gleason score, higher preoperative prostate specific antigen (7.4 vs 5.6 ng/ml), intermediate and high D'Amico classifications, larger tumor volume on magnetic resonance imaging (0.66 vs 0.30 ml), higher PI-RADS® (Prostate Imaging-Reporting and Data System) version 2 category lesions, a greater proportion of intermediate and high grade radical prostatectomy Gleason score lesions, higher pathological T3 stage (all $p < 0.01$) and a higher positive surgical margin rate (19.3% vs 7.8%, $p = 0.016$). On multivariable analysis only tumor volume on magnetic resonance imaging (adjusted OR 1.57, $p = 0.016$), pathological T stage (adjusted OR 2.26, $p = 0.02$), positive surgical margin (adjusted OR 5.0, $p = 0.004$) and radical prostatectomy Gleason score (adjusted OR 2.29, $p = 0.004$) predicted biochemical recurrence.

Conclusions: In this cohort tumor volume on magnetic resonance imaging and pathological variables, including Gleason score, staging and positive surgical margins, significantly predicted biochemical recurrence. This suggests an important new imaging biomarker.

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PROSTATE cancer is the second leading cause of cancer death in men in the United States.[1] Although localized PCa can be definitively treated with RALP, as many as 30% of patients can experience BCR after RALP.[2,3] Various nomograms have been developed to predict BCR after surgery using established preoperative clinical variables such as PSA, biopsy Gleason score and digital rectal examination.[4,5] However, most existing nomograms lack the anatomical and functional information provided by imaging.

As a powerful imaging tool for diagnosis, staging, image guided biopsy and preoperative planning 3TmpMRI has emerged.[6–8] It can provide anatomical, functional and 3D information (ie volumetric data),[9] which is increasingly used to augment existing clinical models to offer improved predictions of biochemical recurrence. Existing studies to date have emphasized qualitative instead of quantitative features,[10] did not use whole mount pathology as a reference standard,[10] used length based measurement such as tumor contact length[11] or studied patients using 1.5 Tesla[12] instead of 3 Tesla MRI.

To our knowledge no studies have evaluated the usefulness of contemporary 3D MRI data (ie 3D MRI volume) and the newer standardized PI-RADS® v2 lexicon combined with state-of-the-art 3TmpMRI to evaluate for biochemical recurrence using whole mount pathology and postoperative PSA as standard references. Therefore, the purpose of this study was to investigate clinical, 3D and conventional quantitative 3TmpMRI predictors using whole mount histopathology as the ground truth to predict BCR after RALP.

METHODS

Study Design

After institutional review board approval and in compliance with the 1996 HIPAA (Health Insurance Portability and Accountability Act) we performed a single arm, observational, single institution study of 395 consecutive patients who underwent 3TmpMRI of the prostate prior to RALP between December 2009 and March 2016. Of the 395 patients 140 lacked followup postoperative PSA and were excluded from analysis. The final study cohort comprised 255 consecutive patients with followup postoperative PSA.

Clinical Information

We collected clinical data (preoperative biopsy Gleason score, patient age and preoperative PSA), MRI information (tumor diameter and volume, prostate volume, solitary vs multifocal tumor, cancer location and PI-RADS v2 category), radical prostatectomy information (Gleason score, pathological stage and positive surgical margins) and clinical outcomes (biochemical recurrence and followup). Biochemical recurrence was defined as postoperative PSA 0.2 ng/ml or greater with an additional PSA 0.2 ng/ml or greater for confirmation when available.[12] The index tumor was defined as the lesion with the highest radical prostatectomy Gleason score on whole mount histopathology. If the patient had a multifocal tumor with the same Gleason score, the tumor with the longest diameter served as the index lesion. Patients were categorized at low, intermediate or high risk according to the standard D'Amico classification.[13]

Magnetic Resonance Imaging

We performed 3TmpMRI using an endorectal coil (MedRAD®) and an external phased array on 1 of several 3 Tesla magnets, including a Trio, Verio or Skyra for 3.0 (Siemens®), in 180 of the 255 patients (70.6%). The remainder underwent external phased array coil mpMRI alone.

The 3TmpMRI protocol included conventional T2W, diffusion-weighted imaging and dynamic contrast enhanced sequences. Images were reviewed with DynaCAD 3 (Philips Invivo®) for 3-dimensional volume of interest delineation of prostate and tumor volumes on T2W. The MRI tumor was contoured on every slice on T2W images and volume was subsequently generated by the software. For all MRI lesions tumor volume was calculated at the time of MRI interpretation by the radiologist. This information was available for referring providers before radical prostatectomy.

Multiparametric Magnetic Resonance Imaging, and Histopathological Analysis and Correlation

Images were interpreted by a single reader, that is 1 of 2 fellowship trained genitourinary radiologists (DJM or SSR) with 8 and 15 years of experience with prostate MRI, respectively. They prospectively identified PCa on preoperative mpMRI. Lesions were then characterized for aggressiveness with PI-RADS v2.[13]

WMHP was analyzed by 1 of 2 dedicated genitourinary pathologists (JH or DYL) with 15 and 4 years of experience with prostate pathology, respectively, while blinded to MRI information. On each section for each individual PCa focus we recorded lesion size, diagrammatic location and Gleason score. In a series of monthly joint sessions 3TmpMRI findings were initially rereviewed and all MRI detected lesions were matched by at least 1 genitourinary radiologist (DJM and/or SSR) with their counterparts on WMHP by at least 1 genitourinary pathologist (DYL and/or JH).

Statistical Analysis

The median and IQR are provided. Differences in continuous variables were measured with the Mann-Whitney U test and categorical variables were measured with the chi-square or the Fisher exact test. Variables significant on univariate analysis were then used in multivariable linear regression. Of the 255 tumors 54