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The role of 3-tesla diffusion-weighted magnetic resonance imaging in selecting prostate cancer patients for active surveillance

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Purpose: Differentiating significant cancer from insignificant cancer is a major challenge in active surveillance (AS) for prostate cancer. We evaluated whether the apparent diffusion coefficient (ADC) grade from 3-T diffusion-weighted magnetic resonance imaging (DW-MRI) is useful to exclude men with unfavorable pathological features from men meeting current AS eligibility criteria.

Methods: Among patients who underwent radical prostatectomy, 117 potential AS candidates defined according to 2013 European Association of Urology guidelines who had undergone preoperative 3-T DW-MRI were included. A blinded uro-radiologist graded the level of suspicion from the ADC map using the Likert scale from 1 to 5. The rate of unfavorable pathological features was evaluated according to ADC grade. Unfavorable pathological features were defined as non–organ-confined disease or pathological Gleason score ≥ 7 (4+3). The associations between unfavorable pathological features and clinical variables including ADC grade (> 3 vs. ≤ 3) were evaluated using logistic regression analysis.

Results: The rates of unfavorable pathological features were 0.0% (0/14), 2.9% (1/34), 5.4% (2/37), 25.0% (6/24), and 37.5% (3/8) from grades 1 to 5 (P = 0.002). The predictive accuracy was as high as 0.804. The rates were significantly different between low (≤ 3, 3.5%) and high (> 3, 28.1%, P < 0.001) grades. The sensitivity, specificity, and positive and negative predictive values were 75.0%, 78.1%, 28.1%, and 96.5%. ADC grade (odds ratio [OR], 10.696; 95% confidence interval [CI], 2.675–42.773) was significantly associated with unfavorable pathological features, even after adjusting for other variables (OR, 11.274; 95% CI, 2.622–48.471).

Conclusions: ADC grade from 3-T DW-MRI is useful to predict men with unfavorable pathologic features from AS candidates.

Keywords: Prostatic neoplasms, Watchful waiting, Pathology, Magnetic resonance imaging

INTRODUCTION

The chief treatment for localized prostate cancer (PC), even very low-risk disease, remains radical prostatectomy (RP) [1,2]. However, autopsy studies have demonstrated that 60%–70% of elderly men have histological PC [3], although only one-third of them are clinically diagnosed before death [4]. Furthermore, from 2.3% to 25% of unselected PC cases may have insignificant pathological features after surgery [5]. Thus, overtreatment is currently a major concern for low-risk localized PC. Publication of the PIVOT trial in particular, has amplified this issue, because RP did not significantly improve overall or disease specific survival compared with observation in the PIVOT trial [6].

Active surveillance (AS) is an attempt to reduce such overtreatment. Early series of AS demonstrated excellent cancer-

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specific and overall survival; however, one-third of patients required definitive treatment during a median 80 months or shorter follow-ups [2,7]. Thus, around one-third of patients might not be offered appropriate treatment at the proper time. Furthermore, longer-term oncological outcomes and quality of life are still unclear. Thus, the major challenge of differentiating those men who have significant cancer from those with insignificant cancer remains unresolved.

Recent reports suggest an emerging role for multiparametric magnetic resonance imaging (MRI) in PC diagnosis [8]. In particular, diffusion-weighted (DW)-MRI has been the focus of interest for its ability to identify aggressive cancer with higher Gleason score [9-12]. However, little is known regarding the role of DW-MRI in selecting PC patients for AS. Thus, we evaluated whether the apparent diffusion coefficient (ADC) grade determined with 3-T DW-MRI is useful for excluding men with unfavorable pathological features from current AS candidates.

MATERIALS AND METHODS

1. Ethics statement

This study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (Seongnam, Republic of Korea). The approval number is B-1307/212-109.

2. Patients

We retrospectively reviewed the patients who underwent RP from January 2008 through April 2013 in Seoul National University Bundang Hospital. The eligibility criteria were AS candidates defined according to 2013 European Association of Urology guidelines (clinical stage T1c-T2a, prostate-specific antigen [PSA] ≤ 10 ng/mL, biopsy Gleason score ≤ 6 [at least 10 cores], ≤ 2 positive cores, ≤ 50% cancer involvement in each core) [2], who had undergone preoperative 3-T multiparametric prostate MRI at our institution. We conducted multiparametric prostate MRI as a routine preoperative evaluation for RP. Almost all patients underwent either 1.5-T or 3-T MRI, and selection of magnetic field strength was determined not by clinical parameters but by schedule of the test. Men who had undergone any kind of neoadjuvant treatment or prior prostate surgery were excluded, because these interventions could affect the MRI reading and pathological outcome.

Among 1,377 men treated with RP during the study period, 25 and 14 patients were excluded because of neoadjuvant therapy and prior prostate surgery, respectively, and 237 patients met AS candidate eligibility according to the above definition. Of these, 117 patients underwent 3-T multiparametric prostate MRI and were included in the final analysis.

3. MRI protocol and ADC grading

All MRI examinations were performed after biopsy, usually 2 to 6 weeks later. MR images were taken using a 3.0-T MR system (Intera Achieva 3.0T, Philips Medical Systems, Best, The Netherlands) equipped with a phased-array cardiac 6-channel coil. In accordance with the recent guideline for prostate MR [13], we did not use an endorectal coil. All patients were injected with 20 mg butylscopolamine (Buscopan, Boehringer Ingelheim Pharma, Ingelheim, Germany) intramuscularly to suppress bowel peristalsis 30 minutes before imaging. Axial DW images were acquired using single-shot echo planar imaging. Scan parameters were as follows: TR, 2,500–3,000 ms; TE, 56–65 ms; slice thickness, 3 mm; interslice gap, 1 mm; field of view, 180 mm × 180 mm; matrix, 92 × 90; and number of excitations, 10. Diffusion encoding gradients were applied as a bipolar pair at b-values 0 and 1,000 s/mm^2. ADC maps were automatically generated on a pixel-by-pixel basis.

An experienced uro-radiologist (S.I.H.), who was blinded to all clinical variables including pathological outcome, independently graded the level of suspicion for clinically significant cancer from ADC mapping images using the Likert scale from 1 to 5 as follows: grade 1, highly unlikely to be present; grade 2, unlikely to be present; grade 3, equivocal; grade 4, likely to be present; and grade 5, highly likely to be present

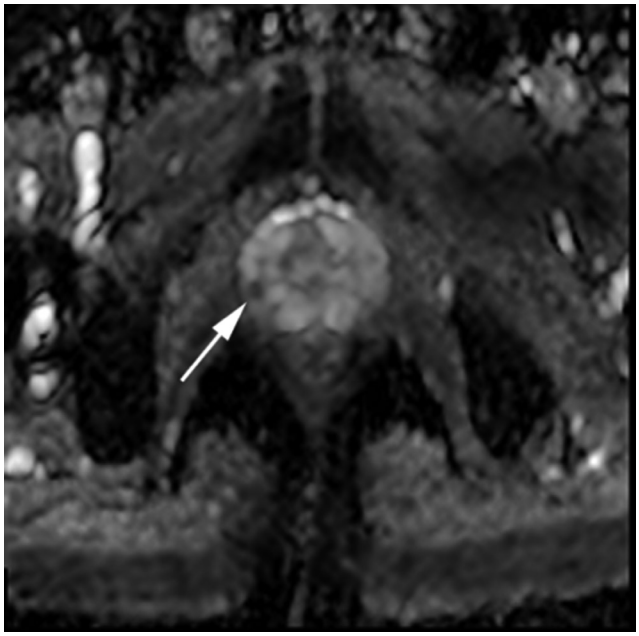

Fig. 1. Axial apparent diffusion coefficient map shows focal low signal intensity nodule (arrow) at right peripheral zone, which was graded 5.

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