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Original Article

Role of Magnetic Resonance Imaging Using Prostate Imaging-Reporting and Data System Version 2 to Predict Clinically Significant Cancer After Radical Prostatectomy in Very Low-Risk or Low-Risk Prostate Cancer

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Purpose: To determine the negative predictive value (NPV) of multiparametric magnetic resonance imaging (mp-MRI) for clinically significant cancer (CSC) based on the Prostate Imaging-Reporting and Data System (PI-RADS) version 2 in very low-risk or low-risk prostate cancer patients.

Materials and Methods: We retrospectively analyzed 380 patients with low risk of prostate cancer who underwent mp-MRI before radical prostatectomy (RP) from 2011 to 2013. Of the 380 patients, 142 patients were in the very low risk group. CSC at RP was defined as follows: any T3–4, G3+4 with tumor volume＞15%, G4+3 or higher. In the very low risk and low risk groups, we analyzed the rate of CSC according to PI-RADS score and calculated the NPV of mp-MRI for detection of CSC.

Results: In the low risk group, 20.8% (n=79) of patients had PI-RADS version 2 score 1–2 and 17.4% (n=66) of patients had PI-RADS version 2 score 3. In the very low risk group, 26.8% (n=38) of patients had PI-RADS version 2 score 1–2 and 17.6% (n=25) of patients had PI-RADS version 2 score 3 in the very low risk group. Rates of CSC were 33.7% (n=128) and 16.9% (n=24) in the low risk and very low risk groups, respectively. The NPV of MRI was 93.7% in the very low risk group and 78.6% in the low risk group.

Conclusions: The NPV of PI-RADS for CSC is high in the very low risk group, but not in the low risk group. Further multicenter studies are needed to investigate the utility of PI-RADS version 2 for NPV. **(Korean J Urol Oncol 2017;15:66-71)**

Key Words: Prostate neoplasms · Magnetic resonance imaging · Prostate Imaging-Reporting and Data System · Prostatectomy

INTRODUCTION

Active surveillance (AS) of low-risk prostate cancer patients is an established option for treatment planning. To select candidates for AS, clinicians have developed several methods that have been compared with regard to effectiveness.[1] Current inclusion criteria for AS of low-risk prostate cancer are typically

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based on prostate-specific antigen (PSA), Gleason score (GS), PSA density (PSAD), clinical staging, and number of positive biopsy cores.[2,3] However, we reported higher percentage rates of upgrading or upstaging in Korean patients based on 6 contemporary AS protocols.[4]

Multiparametric magnetic resonance imaging (mp-MRI) of prostate has demonstrated great promise for detection of prostate cancer and clinically significant cancer (CSC).[5-8] We previously demonstrated that tumor visibility on MRI using a Likert scale is helpful for detecting unfavorable disease.[9] The Prostate Imaging and Report and Data System (PI-RADS) was developed by the European Society of Urogenital Radiology to standardize reporting of mp-MRI in 2012.[10,11] The second version of PI-RADS was introduced to improve MRI interpretation in determining patients who have significant cancer.[12] Several studies showed that mp-MRI is a good modality for prostate cancer risk classification and that it predicts clinically significant cancer before radical prostatectomy (RP) and in AS of prostate cancer.[13,14] However, the clinical utility of PI-RADS version 2 has not been fully validated.

Therefore, the purpose of this study was to analyze whether PI-RADS version 2 can predict CSC after RP in very low risk or low-risk prostate cancer patients.

MATERIALS AND METHODS

1. Data Collection

This retrospective study was approved by the Institutional Review Board of each institution at a single center between 2011 and 2013. A total of 504 patients in the National Comprehensive Cancer Network (NCCN) with low-risk prostate cancer undergoing mp-MRI before RP (GS≤6, PSA＜10 ng/mL, Clinical stage T1c or T2a) were selected and analyzed.[15] Exclusion criteria were as follows: (1) inadequate number of biopsy cores, (2) history of prior hormone or radiation therapy, and (3) inadequate MRI for analysis. Finally, 380 patients with low-risk prostate cancer were retrospectively analyzed. Of the 380 patients, 142 patients were in the very low risk group (GS≤6, PSA＜10 ng/mL, positive cores ≤2, ≤50% of cancer in each core, PSAD＜0.15 ng/mL/g).

2. MRI Technique and Interpretation

All patients underwent mp-MRI with a 3.0T (Intera Achieva TX, Philips Healthcare, Best, The Netherlands) using a phased-array coil without an endo-rectal coil. The routine MRI protocol includes T1-weighted imaging, T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging. One experienced radiologist reviewed MRI using PI-RADS version 2. The PI-RADS version 2 scoring system was defined as follows: score 1, clinically significant cancer is highly unlikely to be present; score 2, clinically significant cancer is unlikely to be present; score 3, the presence of clinically significant cancer is equivocal; score 4, clinically significant cancer is likely to be present; and score 5, clinically significant cancer is highly likely to be present. Nonvisible tumor is PI-RADS version 2 score 1–3 and visible tumor is PI-RADS version 2 score 4–5.[12]

3. Outcomes and Statistical Analyses

In this study, CSC at RP was defined based on a recent study as any T3–4 or G3+4 with tumor volume ＞15% or G4+3 or higher in Korean patients.[16] In the very low risk group and low risk group, rate of CSC was analyzed according to each PI-RADS score using 2 groups (PI-RADS score of 4 or greater and PI-RADS score of less than 4). A p-value of ＜0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA).

RESULTS

Table 1 demonstrates patient characteristics in the low risk and very low risk groups. A total of 380 patients were in the low risk group and 142 patients were in the very low risk group. The mean ages in the low risk and very low risk groups were 64.4 years (range, 42–80 years) and 64.4 years (range, 49–80 years), respectively. The mean prebiopsy PSA in the low risk group and very low risk group were 5.12 ng/mL and 4.21 ng/mL, respectively. Prostate volume in the low risk and very low risk groups were 35 mL (range, 10–89 mL) and 43 mL (range, 19–89 mL), respectively. PSAD in the low risk and very low risk groups were 0.17 ng/mL/g and 0.10 ng/mL/g, respectively. Mean number of positive cores was 2.36 (range, 1–11) and 1.33 (range, 1–2) in the low risk and very low risk groups, respectively. The mean tumor volume (%) was 11% and 7%, respectively. The tumor volume in the low risk and very low risk groups are 3.49 mL and 2.80 mL, respectively.

In the low risk group, there were 20.8% (n=79) PI-RADS

Table 1. Patient characteristics

Characteristic	Low risk group (n=380)	Very low risk group (n=142)
Age (yr)	64.4 (42–80)	64.4 (49–80)
Prebiopsy PSA (ng/mL)	5.12 (0.84–9.89)	4.21 (1.00–9.54)
Prostate volume (mL)	35 (10–89)	43 (19–89)
PSA density (ng/mL/g)	0.17 (0.03–0.63)	0.10 (0.03–0.15)
Positive cores	2.36 (1–11)	1.33 (1–2)
Tumor volume (%)	11 (1–60)	7 (1–40)
Tumor volume (mL)	3.49 (0.04–24.40)	2.80 (0.04–20.75)
MRI, PI-RADS ver. 2 score		
1–2	79 (20.8)	38 (26.8)
3	66 (17.4)	25 (17.6)
4	168 (44.2)	65 (45.8)
5	67 (17.6)	14 (9.9)

Values are presented as mean (range) or number (%).
PSA: prostate-specific antigen, MRI: magnetic resonance imaging, PI-RADS: Prostate Imaging-Reporting and Data System.

Table 2. Rates of clinically significant cancer by PI-RADS version 2 score in low and very low risk groups

Group	Number (%)	Clinically significant cancer*, n (%)
Low risk group	380	128/380 (33.7)
PI-RADS ver. 2 score		
1–2	79 (20.8)	18/79 (22.8)
3	66 (17.4)	13/66 (19.7)
4	168 (44.2)	64/168 (38.1)
5	67 (17.6)	33/67 (49.3)
Very low risk group	142	24/142 (16.9)
PI-RADS ver. 2 score		
1–2	38 (26.8)	2/38 (5.3)
3	25 (17.6)	2/25 (8.0)
4	65 (45.8)	16/65 (24.6)
5	14 (9.9)	4/14 (28.6)

PI-RADS: Prostate Imaging-Reporting and Data System.
*T3–4 or G3+4 with tumor volume >15%, or G4+3 or higher.

Table 3. PI-RADS version 2 scoring performance in the low risk group

Variable	No clinically significant cancer	Clinically significant cancer
No. of nonvisible tumors (n=145)	114	31
No. of visible tumors (n=235)	138	97
Sensitivity (%)	-	75.8
Specificity (%)	-	45.2
Positive predictive value (%)	-	41.2
Negative predictive value (%)	-	78.6

PI-RADS: Prostate Imaging-Reporting and Data System.

Table 4. PI-RADS version 2 scoring performance in the very low risk group

Variable	No clinically significant cancer	Clinically significant cancer
No. of nonvisible tumors (n=63)	59	4
No. of visible tumors (n=79)	59	20
Sensitivity (%)	-	83.3
Specificity (%)	-	50.0
Positive predictive value (%)	-	25.3
Negative predictive value (%)	-	93.7

PI-RADS: Prostate Imaging-Reporting and Data System.

version 2 scores 1–2, 17.4% (n=66) cases of PI-RADS version 2 score 3, 44.2% (n=168) cases of PI-RADS version 2 score 4, and 17.6% (n=67) cases of PI-RADS version 2 score 5. In the very low risk group, there were 26.8% (n=38) cases of PI-RADS version 2 scores 1–2, 17.6% (n=25) cases of PI-RADS version 2 score 3. 45.8% (n=65) cases of PI-RADS version 2 score 4, and 9.9% (n=14) cases of PI-RADS version 2 score 5 (Table 1).

The rates of CSC were 33.7% and 16.9% in the low risk and very low risk groups, respectively, as shown in Table 2. In the low risk group with PI-RADS version 2 scores 1–2, 3, 4, and 5, the rates of CSC were 22.8%, 19.7%, 38.1%, and 49.3%, respectively. In the very low risk group with PI-RADS version 2 scores 1–2, 3, 4, and 5, the rates of CSC were 5.3%, 8.0%, 24.6%, and 28.6%, respectively.

The 2 groups were divided into a nonvisible tumor group

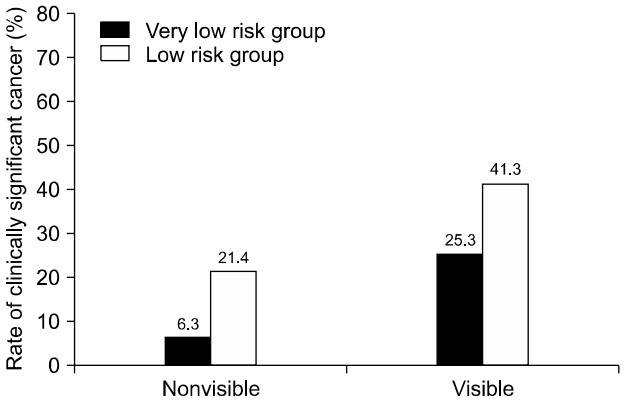

Fig. 1. Rates of clinically significant cancer in patients with nonvisible and visible tumors on magnetic resonance imaging in the very low risk and low risk groups.

(PI-RADS version 2 score 1–3) and visible tumor group (PI-RADS version 2 score 4–5). A total of 21.4% (n=31) patients in the low risk group had nonvisible tumor (PI-RADS version 2 score 1–3) and 6.3% (n=4) patients in the very low risk group had nonvisible tumor (Tables 3, 4 and Fig. 1). There were 41.3% (n=97) of patients with visible tumor (PI-RADS version 2 score 4–5) in the low risk group and 25.3% (n=20) of patients in the very low risk group. The negative predictive value (NPV) of tumor visibility on MRI for CSC is 93.7% in the very low risk group and 78.6% in the low risk group. In the very low risk group, the odds ratio (OR) for visible tumor on MRI in CSC is 5 (95% confidence interval [CI], 1.611–15.518; p=0.003). In the low risk group, the OR is 2.585 (95% CI, 1.608–4.154; $p<0.001$).

DISCUSSION

AS is a conservative management for low-risk prostate cancer that involves careful close monitoring of PSA kinetics and other parameters to delay intervention.[17,18] Published studies regarding AS use criteria based on personal preference and individual clinical experiences. PSA, PSAD, clinical staging, and number of positive biopsy cores have been used to define low-risk prostate cancer.[2,3] The current study follows NCCN guidelines to define low risk group (GS≤6, PSA<10 ng/mL) and very low risk group (GS≤6, PSA<10 ng/mL, positive core ≤2, Max % cancer/core ≤50%, PSAD<0.15 ng/mL/g). It is very important to select appropriate patients for AS. The improved detection abilities of the mp-MRI approach are useful in the AS population.

Several studies have reported the role of tumor invisibility on MRI in AS programs. Margel et al.[19] prospectively enrolled 60 patients with low-risk prostate cancer. They performed mp-MRI and confirmatory prostate biopsy after 1 year. This study highlights that nonvisible tumor on MRI helps clinicians to maintain AS. Mullins et al.[20] reported that mp-MRI had a high NPV (89.7%) for detection of path-index lesions defined as cancer with a given prostate sextant on 2 separate biopsy sessions. In this study, the index lesion on MRI was defined as a single suspicious lesion >10 mm or >2 lesions in a given prostate sextant. Another study by Dianat et al.[21] showed that tumor invisibility on MRI was associated with a lower risk of adverse biopsy pathology. Among men with MRI-invisible tumors, 1 of 12 (8.5%) had pathologically adverse findings and 34 of 84 (40.5%) had adverse pathology in MRI visible tumors. Previously, we also reported that visible tumor in mp-MRI using PI-RADS version 1 was associated with unfavorable disease after RP in candidates for AS.[9] Patients with MRI-visible cancer were more likely to have Gleason upgrading (49.8% vs. 14.3%, $p<0.001$) and unfavorable disease (52.1% vs. 14.3%, $p<0.001$) than patients with MRI-invisible tumor.

Recently, the second version of PI-RADS was designed for detection of clinically significant prostate cancer. Several studies have demonstrated the utility of PI-RADS version 2 in prostate cancer. Vargas et al.[22] reported that PI-RADS version 2 correctly identified 95% of prostate cancer foci ≥0.5 mL. Park et al.[7] demonstrated that PI-RADS score was only a significant factor for CSC. In this study, CSC was defined as follows: (1) surgical GS of 7 or greater, (2) tumor volume of 0.5 cm^3 or greater, or (3) positive extracapsular extension or seminal vesicle invasion. The same group reported that PI-RADS version 2 is helpful for identifying clinically significant cancers in patients with a biopsy GS 6.[23] In their study, the rate of CSC after RP was 87.4% among 182 patients with biopsy Gleason 6. This rate of CSC was very high compared to our study. The rates of CSC in our study were 33.7% and 16.9% in the low risk and very low risk groups, respectively. The difference is the definition of CSC and patient groups. Our study used the definition of CSC (any of T3–4 or G3+4 with tumor volume >15% or G4+3 or higher) validated in Korean patients, which has more pathologically unfavorable findings compared to those of the aforementioned studies.

Assessment of NPV by mp-MRI for detection of clinically significant cancer is usually studied in biopsy settings, not with prostatectomy specimens. Recently, Wang et al.[24] reported that

high grade tumor (GS≥7) was found on transrectal ultrasound (TRUS) biopsy in 10.3% of biopsy-naïve patients (NPV=89.7%), 16.7% of patients with a previous negative biopsy (NPV=83.3%), and 13.3% of patients on AS (NPV=86.6%). The authors suggested that standard template TRUS biopsy is recommended for patients with negative MRI. In contrast, Wysock et al.[25] showed a 98.7% NPV by mp-MRI for high grade tumor (GS≥7) in all patients and a 100% NPV in biopsy naïve patients and those under AS for GS 6.

However, the clinical utility of negative MRI with PI-RADS version 2 has not been fully validated in prostatectomy specimens. Our study found that the NPV of MRI is 78.6% and 93.7% in low risk and very low risk group patients eligible for AS, respectively. Nonvisible tumor on mp-MRI using PI-RADS version 2 in the very low risk group was less likely to be CSC. Therefore, our results suggest that PI-RAD version 2 is helpful in clinical decisions regarding initial AS or definitive treatment.

This study has several limitations. First, the retrospective data were collected at a single institution. Second, we only used the definition of CSC validated in Korean patients in RP specimens. Potentially, clinically significant cancer may be underestimated in our study compared to other studies. Third, we did not evaluate whether the index lesion on mp-MRI corresponded with pathologic lesions on RP specimens, and only one radiologist interpreted the MRI image.

CONCLUSIONS

In the very low risk group, the NPV of multiparametric prostate MRI (PI-RADS version 2) in clinically significant prostate cancer was high, but not in the low risk group. Therefore, tumors that were non-visible on multiparametric prostate MRI appear to be predictive of insignificant prostate cancer in the low risk group. With validation in further studies, multiparametric prostate MRI using PI-RADS version 2 will help to identify candidates for AS in the very low risk group.

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

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