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Complementing the active surveillance criteria with multiparametric magnetic resonance imaging

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Purpose: To evaluate the usefulness of multiparametric magnetic resonance imaging (mpMRI) to avoid misclassification of patients with clinically significant prostate cancer (PCa) into active surveillance (AS).

Materials and Methods: Patients with Gleason grade group (GG) 1 PCa on systematic biopsy who underwent mpMRI before radical prostatectomy (RP) were included. mpMRI and pathologic results were compared between the AS and NOT-AS candidates. Unfavorable disease was defined as the identification of T3-4 disease or GG upgrade in the RP specimen. We established an ideal cutoff Prostate Imaging Reporting and Data System (PI-RADS) score for predicting unfavorable disease, and analyzed the location of index lesions on mpMRI.

Results: PI-RADS scores were not significantly different between AS candidates (n=64) and NOT-AS candidates (n=136; p=0.629). Among 64 AS candidates, GG upgrading and unfavorable disease were diagnosed after RP in 24 (37.5%) and 25 (39.1%) patients, respectively. The rate of unfavorable disease was greater for patients with a PI-RADS score of 5 (83.3%) than in those with a score ≤4 (34.5%; p=0.030). Moreover, most PI-RADS 5 lesions in AS candidates were located in the anterior half of the prostate, with GG upgrading on targeted biopsy in 75.0% of cases.

Conclusions: Among the patients with GG 1 PCa, PI-RADS scores did not differ significantly between AS and NOT-AS candidates. Nonetheless, AS candidates with PI-RADS 5 lesions were diagnosed with unfavorable disease in >80% of RP specimens. Significant cancer located in the anterior half of the prostate including the transitional zone can be missed by systematic biopsy.

Keywords: Image-guided biopsy; Magnetic resonance imaging; Prostatectomy; Prostatic neoplasms

INTRODUCTION

Active surveillance (AS) has become the preferred management strategy for a large proportion of men with low-grade prostate cancer (PCa) [1,2]. The safety of this delayed approach has been demonstrated in multiple large cohort studies with long-term outcomes [3-5]. Although AS has been adopted in national guidelines worldwide [1,2,6], the significant proportion of candidates for AS who may have more aggressive but potentially curable disease remains a specific concern [1]. Early identification of patients with occult aggressive PCa by use of multiparametric magnetic resonance imaging (mpMRI) could improve surveillance results, providing the opportunity for more timely treatment [4,7].

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Based on results of systematic biopsy of the prostate, it is estimated that about 25% of patients with PCa may be improperly placed on AS [8,9], with approximately 50% of patients initially placed on AS requiring treatment owing to pathologic progression or other causes [4]. Therefore, there is a definite need to improve risk stratification, based on systematic biopsy, to minimize the risk for oncologic progression. Recently, attempts have been made to use mpMRI to avoid misclassification to AS [7,10-12] owing to its high detection rate of PCa in combination with its high negative predictive value for significant PCa [12]. In this regard, the relationship between adverse pathologic features and various mpMRI parameters, such as the Prostate Imaging Reporting and Data System ver. 2 (PI-RADSv2) score [13] and apparent diffusion coefficient score, has been analyzed [7,10,11]. However, the mpMRI findings and ideal PI-RADS score cutoffs associated with the diagnosis of unfavorable disease among patients eligible for AS have not yet been fully determined. Accordingly, our study was designed to reduce the misclassification of patients to AS by comparing the results of mpMRI with those from radical prostatectomy (RP) specimen findings. We analyzed whether mpMRI findings can predict unfavorable disease based on pathologic examination of RP specimens among AS candidates with a diagnosis of Gleason grade group (GG) 1 PCa based on systematic biopsy. In addition, we analyzed the mpMRI and MRI/ultrasonography (MRI/US) fusion-targeted biopsy results in misclassified cases who were initially assigned as appropriate for AS.

MATERIALS AND METHODS

1. Statement of research design and ethics

This was a retrospective study of prospectively collected data. Our study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital, with a waiver of written informed consent owing to the retrospective design (approval number: 05-2019-173).

2. Study population

Between January 2015 and December 2019, a total of 348 consecutive men were diagnosed with GG 1 PCa on systematic biopsy and underwent mpMRI, according to the PI-RADSv2 protocol, at our tertiary referral center. Among these patients, the 200 (57.5%) who underwent RP within 6 months after diagnosis were eligible for our study. Overall, 64 of these 200 patients (32.0%) met the Prostate Cancer Research International: Active Surveillance (PRIAS) criteria: GG 1; clinical T-stage ≤T2c; prostate-specific antigen level ≤10 ng/mL; ≤2 positive cores; and prostate-specific antigen density <0.2 ng/mL/mL [14]. The remaining 136 patients (68.0%) had a diagnosis of GG 1 PCa but did not meet the strict PRIAS inclusion criteria for AS. On request of the referring urologist, MRI/US fusion-targeted biopsy (103 of 200) was combined with an additional transrectal ultrasound-guided systematic biopsy.

3. mpMRI and MRI/US fusion-targeted biopsy

At our institution, all included patients undergo 3.0-T MRI (Intera Achieva 3.0 T; Phillips Medical System, Best, Netherlands), with a dedicated a phased-array coil (six channels). In alignment with the PI-RADSv2 guidelines [13], our mpMRI protocol includes T2-weighted imaging, dynamic contrast-enhanced imaging, and diffusion-weighted imaging with apparent diffusion coefficient reconstruction. All mpMRI results were reviewed by one urogenital radiologist (TUK), who had >5 years of experience in reviewing prostate MR images at the start of this study. Individual lesions were scored by using the PI-RADSv2 5-point likelihood scale for significant PCa [13].

The BioJet® Fusion Biopsy System (D&K Technologies GnbH, Barum, Germany) was used to superimpose labeled T2-weighted MR images over the real-time transrectal ultrasound images to facilitate identification of target lesions. Three biopsy cores were subsequently obtained for each target lesion, using a transrectal or transperineal approach under visual guidance using the BioJet® device. Targeted biopsy was performed before systematic biopsy, within the same session.

4. Pathologic review

One expert uropathologist (HJL) reviewed and described all biopsy cores and RP specimens. For each positive biopsy core, the Gleason score and the percentage of involvement of the core length were reported. All RP specimens were reviewed using a whole-mount technique, with the modified Gleason score used to grade identified PCa lesions, as per the 2014 recommendations of the International Society of Urological Pathology [15]. The Gleason score upgrading was defined by changes from GG 1 to GG 2–5 PCa. Unfavorable disease based on the RP specimen was defined if pathologic T3-4 or Gleason score upgrading was diagnosed.

5. Statistical analysis

Demographic, clinical, radiological, and pathologic results of patients with GG 1 PCa on systematic biopsy were compared between the AS and NOT-AS group by using chi-squared test for categorical variables and Student's t-test for continuous variables. To evaluate the ideal cutoff of the PI-

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Table 1. Comparison of demographic, radiological, and pathologic characteristics in patients with Gleason grade group 1 prostate cancer by systematic prostate biopsy and who are candidates for AS according to the PRIAS guidelines or not

Variable	AS candidate (n=64)	NOT-AS candidate (n=136)	p-value
Age (y)	65 (59–68)	65 (59–70)	0.637
PSA (ng/mL)	5.0 (4.4–5.6)	7.3 (5.1–10.0)	<0.001
PSA density (ng/mL^2)	0.140 (0.090–0.153)	0.239 (0.136–0.281)	<0.001
Prostate volume (mL)	39 (30–46)	33 (23–39)	0.002
PI-RADS score			0.629
2	3 (4.7)	3 (2.2)	
3	23 (35.9)	45 (33.1)	
4	32 (50.0)	69 (50.7)	
5	6 (9.4)	19 (14.0)	
No. of tumor cores on systematic biopsy			<0.001
≤2	64 (100.0)	57 (41.9)	
3	-	34 (25.0)	
≥4	-	45 (33.1)	
% Maximum tumor core	16 (8–20)	30 (13–40)	<0.001
Pathology at radical prostatectomy specimen			
% Tumor volume	5 (3–8)	10 (5–15)	<0.001
Organ-confined disease	57 (89.1)	100 (73.5)	0.016
Extracapsular extension	6 (9.4)	36 (26.5)	0.005
Seminal vesicle invasion	1 (1.6)	4 (2.9)	1.000
Pathologic Gleason score			<0.001
6	40 (62.5)	45 (33.1)	
7	22 (34.4)	87 (64.0)	
8	2 (3.1)	4 (2.9)	
Unfavorable pathology[a]	25 (39.1)	93 (68.4)	<0.001
Oncological outcome			
Biochemical recurrence	2 (3.1)	11 (8.1)	0.180
Metastasis	-	3 (2.2)	0.230
Local recurrence	-	-	-

Values are presented as median (95% confidence interval) or number (%).
AS, active surveillance; PRIAS, Prostate Cancer Research International: Active Surveillance; PSA, prostate-specific antigen; PI-RADS, Prostate Imaging Reporting and Data System.
[a]:Unfavorable disease, not organ-confined disease or Gleason grade group ≥2.

RADS score for assignment to AS, the pathologic results of RP specimen of AS candidates were compared between PI-RADS ≤3 and 4–5 (and between PI-RADS ≤4 and 5) using Fisher's exact test.

In addition, the clinical and radiological characteristics of AS candidates were further analyzed and compared between patients with unfavorable disease and those with favorable disease (GG 1 and organ-confined disease at RP specimen). Between-group differences were evaluated using the chi-squared test for categorical variables and Student's t-test for continuous variables. In AS candidates with PI-RADS 4–5 lesions, we analyzed the location of the index lesions on mpMRI and the results of MRI/US fusion-targeted biopsy. All statistical analyses were performed using PASW Statistics (ver. 18.0; IBM Corp., Armonk, NY, USA), with a p-value <0.05 deemed significant.

RESULTS

As shown in Table 1, all clinical and pathologic data of patients with GG 1 PCa differed significantly between AS candidates (n=64) and NOT-AS candidates (n=136), except for age and PI-RADS score. The distribution of PI-RADS scores of 2, 3, 4, and 5 did not differ significantly between AS candidates (4.7%, 35.9%, 50.0%, and 9.4%, respectively) and NOT-AS candidates (2.2%, 33.1%, 50.7%, and 14.0%, respectively; p=0.629). The rate of pathologic Gleason score upgrading in AS candidates and NOT-AS candidates was 37.5% (24 of 64) and 66.9% (91 of 136), respectively (p<0.001). Unfavorable disease in AS candidates and NOT-AS candidates was

Table 2. Pathologic characteristics after radical prostatectomy according to PI-RADS score in patients with low-risk prostate cancer and Gleason score 6 on biopsy

Variable	PI-RADS score			
	2	3	4	5
Pathologic Gleason score				
3+3	2 (2.3)	37 (42.0)	45 (51.1)	4 (4.5)
3+4	4 (2.9)	49 (35.3)	66 (47.5)	20 (14.4)
4+3	0 (0.0)	19 (24.4)	47 (60.3)	12 (15.4)
3+5	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)
4+4	0 (0.0)	4 (10.5)	20 (52.6)	14 (36.8)
4+5	0 (0.0)	0 (0.0)	8 (50.0)	8 (50.0)
5+4	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
% Tumor volume	4 (3–25)	8 (3–12)	13 (7–20)	25 (15–36)

Values are presented as number (%) or median (95% confidence interval).
PI-RADS, Prostate Imaging Reporting and Data System.

Table 3. Comparison of pathologic outcome in active surveillance candidates using various PI-RADS cutoffs

Variable	Active surveillance candidates using PRIAS criteria (n=64)						
	Overall	PI-RADS ≤3	PI-RADS 4–5	p-value	PI-RADS ≤4	PI-RADS 5	p-value
No. of patients	64	26	38		58	6	
Gleason score upgrade	24 (37.5)	9 (34.6)	15 (39.5)	0.573	20 (34.5)	4 (66.7)	0.072
Organ-confined disease	57 (89.1)	25 (96.2)	32 (84.2)	0.225	52 (89.7)	5 (83.3)	0.516
Extracapsular extension	6 (9.4)	1 (3.8)	5 (13.2)	0.387	5 (8.6)	1 (16.7)	0.460
Seminal vesicle invasion	1 (1.6)	0 (0.0)	1 (2.6)	1.000	1 (1.7)	0 (0.0)	1.000
Unfavorable disease[a]	25 (39.1)	9 (34.6)	16 (42.1)	0.609	20 (34.5)	5 (83.3)	0.030

Values are presented as number only or number (%).
PI-RADS, Prostate Imaging Reporting and Data System; PRIAS, Prostate Cancer Research International: Active Surveillance.
[a]:Unfavorable disease, not organ-confined disease or Gleason grade group ≥2.

diagnosed in 25 (39.1%) and 93 (68.4%), respectively (p<0.001). Seminal vesicle invasion and extracapsular extension was diagnosed in 1 (1.6%) and 6 (9.4%) AS candidates, respectively, compared with 4 (2.9%) and 36 (26.5%) NOT-AS candidates, respectively. The rate of biochemical recurrence after RP was 3.1% in AS candidates, compared with 8.1% in NOT-AS candidates. During follow-up, metastasis was diagnosed in 3 NOT-AS candidates (2.2%). Pathologic characteristics of RP specimens are described in Table 2.

Comparing the patients with PI-RADS ≤3 vs. 4–5, the proportion of unfavorable disease in each group was not significantly different: 9 of 26 (34.6%) and 16 of 38 (42.1%), respectively (p=0.609) (Table 3). Gleason score upgrading in each group was also not significantly different (34.6% vs. 39.5%; p=0.573). However, when comparing the patients with PI-RADS ≤4 vs. 5, the proportion of unfavorable disease did differ significantly: 20 (34.5%) and 5 (83.3%), respectively (p=0.030). Negative predictive values of favorable disease in patients eligible for AS were 0.42 (16/38) using the cutoff PI-RADS score of ≤3; however, these values were 0.83 (5/6) using the cutoff PI-RADS score ≤4. Therefore, the patients with PI-RADS 5 lesions were not suitable for AS.

Differences in the demographic, clinical, radiological, and pathologic characteristics of patients with unfavorable disease compared with those with favorable disease, based on RP specimen examination, are reported in Table 4. The median age of the unfavorable disease group was higher than that of the favorable disease group (p=0.016). The number of positive cores was higher in the unfavorable disease group than in the favorable disease group (p=0.046). However, the distribution of PI-RADS scores was not significantly different (p=0.141).

The location of index lesions in patients with PI-RADS 4–5 lesions is reported in Table 5. Particularly, the PI-RADS 5 lesion in this population was located in the anterior half of the prostate (66.7%) and the transitional zone (100%) and diagnosed as unfavorable disease in 83.3% cases (5 of 6) (Fig. 1).

MRI/US fusion-targeted biopsy was performed in 62.5% (20 of 32) of cases with a PI-RADS 4 lesion and in 66.7% (4 of 6) of cases with a PI-RADS 5 lesion. Based on the targeted biopsy before RP, upgrading was confirmed in 6 of 20 (30.0%)

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Table 4. Comparison of demographic, clinical, and pathologic characteristics in candidates for active surveillance with unfavorable or favorable disease characteristics after radical prostatectomy

Variable	Unfavorable disease[a]	Favorable disease	p-value
No. of patients	25	39	
Age (y)	68 (65–72)	64 (60–67)	0.016
Preoperative PSA (ng/mL)	5.1 (4.4–6.0)	5.0 (4.5–6.9)	0.720
Prostate volume (mL)	34 (28–47)	42 (34–51)	0.076
PSA density (ng/mL^2)	0.15 (0.12–0.16)	0.14 (0.09–0.16)	0.193
Positive core among systematic biopsy			0.046
1	12 (48.0)	28 (71.8)	
2	13 (52.0)	11 (28.2)	
% Maximum tumor core	19 (13–34)	13 (10–20)	0.141
PI-RADS score			0.141
2	1 (4.0)	2 (5.1)	
3	8 (32.0)	15 (38.5)	
4	11 (44.0)	21 (53.8)	
5	5 (20.0)	1 (2.6)	
Pathology of radical prostatectomy specimen			
Positive surgical margin	3 (12.0)	-	0.055
Organ-confined disease	18 (72.0)	39 (100.0)	0.001
Extracapsular extension	6 (24.0)	-	0.002
Seminal vesicle invasion	1 (4.0)	-	0.391
% Tumor volume	10 (5–15)	3 (2–5)	<0.001
Pathologic Gleason score			<0.001
GG 1	1 (4.0)	39 (100.0)	
GG 2	21 (84.0)	-	
GG 3	1 (4.0)	-	
GG 4	2 (8.0)	-	

Values are presented as number only, median (interquartile range), or number (%).
PSA, prostate-specific antigen; PI-RADS, Prostate Imaging Reporting and Data System; GG, Gleason grade group.
[a]:Unfavorable disease, not organ-confined disease or Gleason grade group ≥2.

Table 5. Comparison of location of index lesion on multiparametric magnetic resonance image and results of targeted biopsy in active surveillance candidates with PI-RADS 4–5 lesions

Variable	PI-RADS 4	PI-RADS 5
No. of patients	32	6
Index lesion located in anterior half of the prostate	15 (46.9)	4 (66.7)
Index lesion located in transitional zone	16 (50.0)	6 (100)
Unfavorable disease[a]	11 (34.4)	5 (83.3)
Targeted biopsy	20 (62.5)	4 (66.7)
Upgrading in targeted biopsy	6 (30.0)	3 (75.0)

Values are presented as number only or number (%).
PI-RADS, Prostate Imaging Reporting and Data System.
[a]:Unfavorable disease, not organ-confined disease or Gleason grade group ≥2.

AS candidates with a PI-RADS 4 lesion and in 3 of 4 (75.0%) AS candidates with a PI-RADS 5 lesion.

DISCUSSION

The usefulness of the PI-RADS score for appropriately selecting candidates for AS was limited in our study. Among patients diagnosed with GG 1 PCa by systematic biopsy, the PI-RADS scores did not differ significantly between AS and NOT-AS candidates (p=0.629). Furthermore, even when compared with the final pathology findings after RP, the value of the PI-RADS score was less in most AS candidates. Only PI-RADS 5 lesions were associated with unfavorable disease after RP in patients initially deemed eligible for AS, resulting from a low rate of detection of PI-RADS 5 lesions located in the anterior half of the prostate including the transitional zone. Unfortunately, most candidates for AS (90% in this study) have PI-RADS ≤4 lesions. We also note that in previous studies, lesions in patients with GG 1 PCa were reported to be largely invisible on mpMRI [16-18]. Therefore, although several studies have reported mpMRI to be useful for the selection of candidates appropriate for AS [19,20], mpMRI

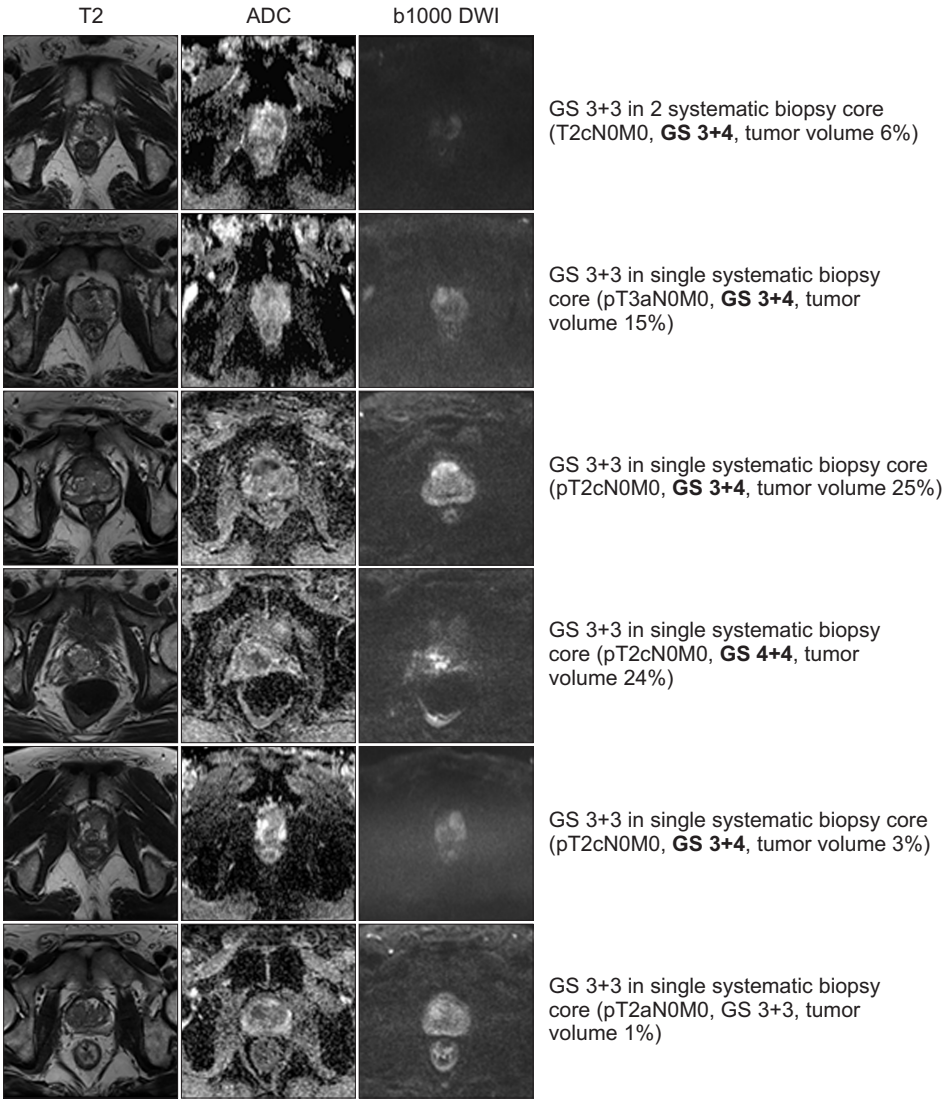

Fig. 1. Five of six active surveillance candidates with PI-RADS 5 lesions diagnosed by Gleason score upgrading in the radical prostatectomy specimen. Most PI-RADS 5 lesions in active surveillance candidates were located in the anterior part of the prostate, including the transitional zone. PI-RADS, Prostate Imaging Reporting and Data System; ADC, apparent diffusion coefficient reconstructions; DWI, diffusion-weighted imaging; GS, Gleason score.

may, in fact, be reliable only for candidates with GG ≥2 lesions.

AS is currently recognized as a standard of care in patients with low-risk PCa. However, misclassification has always been a concern. The probability of upgrading after confirmatory biopsy is approximately one-quarter [8]. This considerable obstacle has not yet been overcome. Recently, as mpMRI technology has developed, its use in candidates for AS has increased [19], with one study having evaluated the possibility of mpMRI as a substitute for follow-up biopsy for patients on AS [21]. Furthermore, adding the fusion biopsy technique to mpMRI helps to detect cancer more accurately [22].

Since the introduction of mpMRI for PCa, mpMRI and PI-RADS scoring have been used as screening criteria for AS [7,19,20]. Zhai et al. [19] reported that the pooled estimates of PI-RADS scores of 4 or 5 predicted adverse pathologic features on examination of RP specimens among AS candidates, based on the PRIAS criteria, with a sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve of 0.77, 0.63, 0.72, 0.68, and 0.77, respectively. Based on their analysis, Zhai et al. [19] proposed that patients with PI-RADS scores of 4-5 would be unsuitable for AS, with AS being a relatively safe management strategy for patients with a PI-RADS score ≤3. Kim et al. [7] reported that multiple PI-RADS 5 lesions were strongly associated with GG 3 or pathologic T3 disease. Mamawala et al. [20] reported 2- and 4-year upgrade-free survival rates of 93% and 83%, 74% and 59%, and 87% and 76%, respectively, for negative mpMRI, positive mpMRI (PI-RADS ≥3), and pre-mpMRI era, respectively ($p<0.001$). In a multivariable analysis, positive mpMRI findings (defined by a PI-RADS score ≥3) predicted a significantly higher rate of GG upgrading than did negative mpMRI findings with a hazard ratio for GG upgrading of 0.61 ($p=0.030$) for negative mpMRI findings compared with 1.96 ($p<0.001$) for positive mpMRI findings [20]. However, the

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appropriate cutoff PI-RADS score for AS remains controversial. In our study, the negative predictive value of favorable disease among patients eligible for AS was 0.42 (16/38) using a cutoff PI-RADS score ≤3 and 0.83 (5/6) using a cutoff PI-RADS score of ≤4. Therefore, a PI-RADS score ≤4 provided a more ideal cutoff than a PI-RADS score ≤3 for selecting candidates appropriate for AS.

Siddiqui et al. [23] reported a greater association between Gleason score upgrading and targeted rather than systematic biopsy. Adding targeted biopsy led to upgrading in 81 (32%) cases. Moreover, targeted biopsy detected 67% more GG ≥3 tumors than systematic biopsy alone but did miss 36% of GG ≤2 tumors, thus mitigating its utility for lower-grade disease. By comparison, systematic biopsy led to upgrading in 67 (26%) cases over targeted biopsy alone, but detected only 8% more GG ≥3 tumors. In their analysis of the utility of concomitant-targeted biopsy for predicting favorable disease in RP specimens among several AS cohorts, Ploussard et al. [24] concluded that negative targeted biopsy results were strongly associated with the absence of final GG ≥3 disease. Tumor grade on targeted biopsy significantly correlated with the risk of a final GG ≥3 in both the Toronto and UCSF cohorts, but not in the PRIAS cohort. The ASIST trial was designed to test the hypothesis that targeted biopsy would identify more men with GG ≥2 cancer than systematic biopsy among AS candidates with GG 1 PCa [25,26]. However, initial results from this trial did not support this hypothesis, with 23% of patients in the systematic biopsy group identified as having GG ≥2 cancer at the time of confirmatory biopsy compared with 21% of patients in the MRI arm (targeted+systematic biopsy) [26]. After a 2-year follow-up, however, baseline mpMRI, before confirmatory biopsy, yielded 50% fewer failures of surveillance and less progression to higher-grade cancer [25]. Ahdoot et al. [18] reported on the diagnostic accuracy of targeted, systematic, and combined biopsy for lesions visible on MRI, with MRI-targeted biopsy providing a greater diagnostic yield than systematic biopsy. Specifically, 134 men with a diagnosis of GG 1 cancer by systematic biopsy were upgraded to a GG ≥2 cancer on MRI-targeted biopsy. Simultaneously, MRI-targeted biopsy led to 74 new GG 1 cancer diagnoses among men in whom no cancer was detected by systematic biopsy. Thus, overall, MRI-targeted biopsy yielded GG upgrading in 458 patients (21.8%) when added to systematic biopsy.

Several previous studies have reported on the risk of tumors located anteriorly in the prostate being overlooked among AS candidates. Specifically, a large proportion of high-grade tumors in the anterior prostate missed by systematic biopsy can be identified using transperineal template-guided prostate biopsy [27-30]. According to Ayres et al. [27], of a total of 29% of men with Gleason score upgrading after transperineal template prostate biopsy among AS candidates, the cancer was upgraded from a GG 1 to a GG 2 in 22% of cases, a GG 1 to a GG 3 in 5% of cases, and a GG 1 to a GG ≥4 in 2% of cases. Of these patients, 44% had a lesion located in the anterior zone of the prostate [27]. Lee et al. [28] reported similar results, with a higher Gleason score identified in 29.3% of AS candidates after transperineal template-guided biopsy, with the cancer being upgraded from a GG 1 to a GG 2 in 19.2% of cases, a GG 1 to a GG 3 in 6.1% of cases, and a GG 1 to a GG ≥4 in 4% of cases. Among these patients, 51.7% had a lesion located in the anterior part of the prostate, and 75.9% had a lesion located either in the anterior or the apical zone of the prostate. Among patients who had previous negative biopsy results, a tumor location in the anterior part of the prostate was also an important factor. Nafie et al. [30] reported a 58% cancer detection rate after transperineal template-guided prostate biopsy among patients with previous double-negative transrectal systematic biopsy. Of these patients, 39%, 48%, 7%, and 6% had GG 1, 2, 3, and 5 cancer, respectively. Among the positive cores, 49% were found in the anterior part of the prostate. Gershman et al. [29] reported a 50% cancer detection rate after transperineal template-guided prostate biopsy in cases with previous negative transrectal and transurethral resection biopsies. Among these, GG 1 cancer was detected in 52.9% of cases and GG ≥2 in 47.1% of cases. Of these, 82.4% had cancer in the anterior part of the prostate, 52.9% in the apical prostate, and 94.1% in either the anterior or the apical prostate.

The limitations of our study need to be acknowledged. Foremost, this was a retrospective single-institution study and, therefore, a selection bias for RP or targeted biopsy is inevitable. Our findings will require validation by a large randomized controlled clinical trial. Second, the patients in our study group, who underwent both RP and mpMRI, represent a small component of the overall AS cohort, which may have skewed the true prevalence of PCa in this population. Finally, the effect of the diagnostic accuracy of using combined mpMRI with PI-RADSv2 may have been underestimated in our study, as the detailed pathologic data, location, number, or size of the lesion in the RP specimens were not directly compared with the mpMRI results.

CONCLUSIONS

The usefulness of mpMRI was limited in patients with low-grade PCa, including those who were candidates for AS. Among patients with low-grade PCa, the PI-RADS score was

not significantly different between AS and NOT-AS candidates. Of note, the PI-RADS score was also not significantly different between patients with unfavorable disease and those with favorable disease in the RP specimen. However, AS candidates with PI-RADS 5 lesions were associated with unfavorable disease after RP. Because the PI-RADS 5 lesion in AS candidates was mostly located in the anterior half of the prostate, including the transitional zone, systematic biopsy was insufficient. Hence, targeted biopsy with mpMRI will be more strongly recommended in the future for choosing candidates for AS.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Tae Un Kim and Sung-Woo Park. Data acquisition: Tae Un Kim, Seung Ryong Baek, Won Hoon Song, Jong Kil Nam, Hyun Jung Lee, and Sung-Woo Park. Statistical analysis: Tae Un Kim and Sung-Woo Park. Data analysis and interpretation: Tae Un Kim and Sung-Woo Park. Drafting of the manuscript: Tae Un Kim and Sung-Woo Park. Critical revision of the manuscript: Seung Ryong Baek, Won Hoon Song, Jong Kil Nam, and Hyun Jung Lee. Obtaining funding: Tae Un Kim, Hyun Jung Lee, and Sung-Woo Park. Administrative, technical, or material support: Tae Un Kim, Hyun Jung Lee, and Sung-Woo Park. Supervision: Tae Un Kim, Hyun Jung Lee, and Sung-Woo Park. Approval of the final manuscript: Tae Un Kim, Seung Ryong Baek, Won Hoon Song, Jong Kil Nam, Hyun Jung Lee, and Sung-Woo Park.

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