MRI suspicious lesions in patients under active surveillance

Do systematic biopsies still add value?

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ABSTRACT

INTRODUCTION: Active surveillance (AS) requires regular monitoring to detect disease progression. Multiparametric magnetic resonance imaging (mpMRI) and targeted biopsies are commonly used to identify clinically significant prostate cancer (csPC) in AS patients, yet their diagnostic value remains unclear among this population.

METHODS: We conducted a retrospective study of patients who underwent mpMRI followed by combined prostate biopsies between 2017 and 2022. Patients were categorized into AS and non-AS groups. We compared the diagnostic yield of mpMRI suspicious Prostate Imaging-Reporting & Data System (PI-RADS) 3–5 lesions using comparisons of PI-RADS score distribution and detection rates of csPC from targeted biopsies between the groups. Logistic regression was used to assess associations between AS category and outcomes. csPC detection rates of targeted and combined biopsies were also assessed.

RESULTS: The study consisted of 600 patients, 158 in the AS group and 442 in the non-AS group. PI-RADS score distribution and the number of suspicious lesions were similar between AS and non-AS groups. csPC detection rates from targeted biopsies were not different between AS and non-AS patients (32% vs. 30%, p=0.68), and AS was also not associated with the rates of csPC for each PI-RADS score. The addition of systematic biopsies did not increase csPC detection in AS patients (36% vs. 32%, p=0.47).

CONCLUSIONS: Our findings suggest that mpMRI suspicious PI-RADS 3–5 lesions are reliable for csPC diagnosis during AS, and that targeted biopsies alone may be sufficient for its detection; however, further prospective research is needed to validate these results and optimize biopsy strategies within AS protocols.

INTRODUCTION

Treatment options for low-risk prostate cancer (PCa) are diverse, including active surveillance (AS), radiation therapy, and radical prostatectomy. The choice of treatment depends significantly on the patient's life expectancy and personal preferences, emphasizing the importance of a shared decision-making process between the patient and their physician.

The literature consistently demonstrates that AS provides equal oncologic outcomes and minimizes treatment-related complications and toxicity, establishing it as the preferred approach for these low-risk patients.[1,2] Nevertheless, low-risk PCa can progress to clinically significant stages over time, albeit typically after many years. Thus, AS involves frequent monitoring to detect subclinical progression early, allowing for timely intervention before disease dissemination. Approximately 20% of patients initially diagnosed with low-risk disease already exhibit additional significant foci within the prostate, and an annual progression rate of 1–2% underscores the need for vigilant surveillance.[3,4] Various factors, such as age, genetic testing outcomes, and disease volume, may influence the decision to pursue definitive treatment.

The protocol for AS varies among healthcare organizations and may include a range of periodic assessments, such as serum prostate-specific antigen (PSA) levels, rectal examinations, multiparametric magnetic resonance imaging (mpMRI), and repeat biopsies.[5] Inconsistencies exist in both frequency and quality of these assessments, specifically

regarding the utility of mpMRI and targeted biopsies.[6-8] Following the rationale that patients with already known insignificant PCa may harbor less significant disease in their mpMRI suspicious lesions, our study aimed to evaluate the diagnostic yield of suspicious lesions on mpMRI among AS patients who underwent combined biopsies.

METHODS

Patients

After obtaining institutional review board approval, we conducted a retrospective study that included patients who had mpMRI of the prostate, suspicious lesions classified as Prostate Imaging-Reporting and Data System v2.1 (PI-RADS) score ≥3, and underwent combined (targeted and systematic) transperineal prostate biopsies in our institution between March 2017 and March 2022. All patients in the cohort performed their mpMRI due to elevated levels of PSA, abnormal rectal examination, or AS. We excluded patients whose suspicious lesions were either not classified or classified as PI-RADS score ≤2, those who did not perform a combined biopsy, and those with no pathologic report. Patients who were on AS protocol after a confirmatory biopsy for at least six months at the time of the mpMRI scan were considered the AS group of our study.

Study design and outcomes

To evaluate the diagnostic yield of suspicious lesions on mpMRI among AS patients who underwent combined biopsies, we compared their diagnostic outcomes to non-AS patients. Outcomes included PI-RADS score distribution, number of suspicious lesions, the detection rates of clinically significant PCa from the targeted biopsies (targeted-csPC) and from the combined biopsies (combined-csPC), and the diagnosis of any cancer. To address the contribution of systematic biopsies, csPC and any cancer detection rates were also compared between targeted and combined biopsies in each group.

Our sample size calculation was based on prior studies assessing csPC detection rates of combined and targeted biopsies, the prediction for 1:3 ratio between AS and non-AS patients, and ensuring a statistical power of 80% and significance level (alpha) of 0.05. We found that 412 patients would be needed to show a difference of 15% in targeted-csPC rates between the groups. In cases of multiple suspicious lesions on mpMRI, the higher PI-RADS score was considered for analysis. csPC was defined as International Society of Urological Pathologists (ISUP) ≥2, insignificant cancer as ISUP=1; the highest ISUP score was considered for analyses.

mpMRI protocol and biopsy technique

The mpMRI scans were conducted using a 3T scanner equipped with a 16-channel surface coil. In adherence to PI-RADS guidelines, the scanning protocol included T2-weighted sequences in three planes, T1 volumetric interpolated sequences both pre- and post-contrast administration, and diffusion-weighted imaging (DWI) sequences in the axial plane. The relative apparent diffusion coefficient (ADC) map was also calculated. Each identified lesion was assigned a PI-RADS score based on its mpMRI characteristics.

Our protocol for transperineal fusion biopsies combines MRI-targeted and systematic samplings from the peripheral, anterior, and apical zones. The procedure begins with the patient under general or regional anesthesia in the lithotomy position. A biplanar transrectal ultrasound (TRUS) probe (BK Medical, Peabody MA, U.S.) mounted on a flexible arm (D&K Technologies GmbH, Barum, Germany) is inserted. The mpMRI and TRUS images are fused using the BioJet system (D&K Technologies GmbH, Barum, Germany). Suspected lesions and the prostate contour are outlined on the mpMRI image and overlaid on the TRUS image.

Biopsies are performed transperineally using a 5 mm grid and a spring-loaded biopsy gun with an 18 G needle. The procedures are conducted by one of three urologists with several years of experience using the BioJet MRI/TRUS fusion biopsy system. After targeting all suspicious lesions, systematic biopsies are obtained. Cores from the peripheral zone are sampled using the extended 12-core scheme, while the anterior zone and the mid-anterior apex are directly sampled using the Ginsburg protocol.[9,10] Each core is then assessed for the ISUP grade group by a dedicated genitourinary pathologist.[11]

Statistical analysis

Statistical comparisons between AS and non-AS groups were performed by Chi-squared, Fisher-exact, and Mann-Whitney U tests. McNemar's test was performed to compare between targeted and systematic samplings in a matched manner within the groups. Logistic regressions were performed to calculate the association between variables and outcomes. All analyses were two-sided, and statistical significance was defined as $p<0.05$. The statistical analyses were done with SPSS v. 29 (IBM, U.S.) and the figures were created using Microsoft Excel.

RESULTS

Study population

The cohort included 600 consecutive patients who fulfilled the inclusion criteria and did not meet the exclusion criteria, and 158 patients were qualified for the AS group. The median age and median PSA level of the cohort were 73 years (interquartile range [IQR] 63–73) and 6.60 ng/dL (IQR 4.91–9.47), respectively. The median prostate volume as measured by the mpMRI was 55 mL (37–79), and 77% of the patients were staged as cT1 following rectal examination. Table 1 presents coma parison of baseline characteristics between the study groups. All baseline characteristics, including age, PSA, prostate volume, cT staging, family history of prostate cancer, and 5-alpha-reductase inhibitors treatment, were similar between the groups.

Table 1. Comparison of baseline characteristics between AS categories

Characteristic	AS group (n=158)	Biopsy-naive group (n=442)	p
Age (years)	69 (64–73)	69 (63–73)	0.36
PSA (ng/dL)	6.76 (4.88–10)	6.60 (4.97–6)	0.55
Prostate volume (ml)	54 (39–70)	55 (37–81)	0.39
Clinical T stage			0.19
T1	125 (79%)	339 (77%)	
T2	33 (21%)	94 (21%)	
T3	0	9 (2%)	
Family history	16 (10%)	67 (15%)	0.14
5-ARI treatment	15 (9%)	37 (8%)	0.74

The continuous variables are reported as medians (IQR) and the categorical variables as numbers (%). ARI: alpha reductase inhibitor; AS: active surveillance; PSA: prostate-specific antigen.

PI-RADS scores and number of suspicious lesions

The prevalences of PI-RADS scores of 3, 4, and 5 among the cohort were 24% (145 patients), 56% (336 patients), and 20% (119 patients), respectively. Most patients had multiple suspicious lesions (334 patients, 56%), and 266 (44%) had a solitary one. The rates of PI-RADS scores 3, 4, and 5 were 23%, 58%, and 19%, respectively, among the AS group, and 25%, 55%, and 20%, respectively, among the non-AS group (p=0.82) (Figure 1). The number of suspicious lesions on mpMRI per patient was also not different between the AS categories (p=0.23), as 50%, 34%, and 16% had one, two, or three or more lesions, respectively, in the AS group, and 43%, 40%, and 17%, respectively, in the non-AS group. AS was not associated with PI-RADS ≥4 score on univariate logistic regression analysis (odds ratio [OR] 1.1, 95% confidence interval [CI] 0.7–1.7, p=0.67).

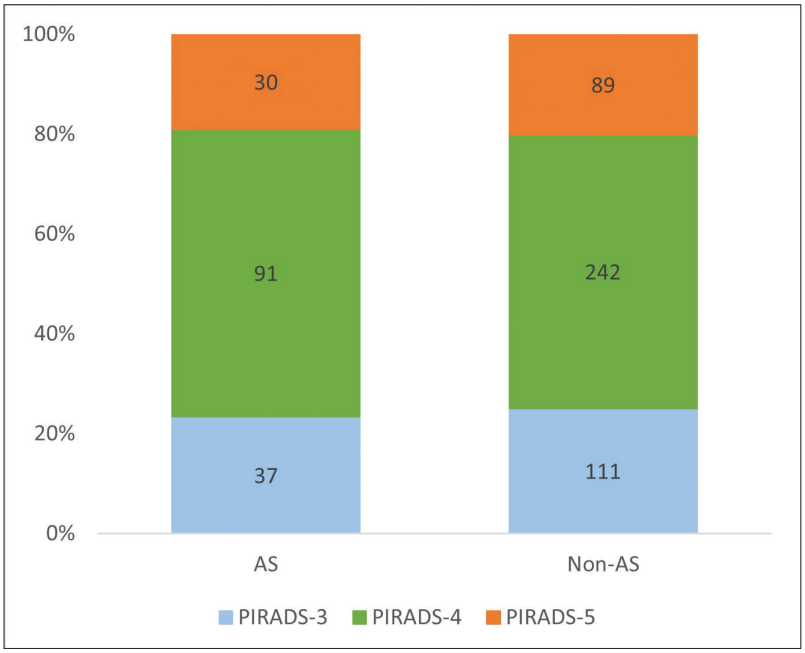

Figure 1. Comparison of PI-RADS scores between AS categories. Numbers in boxes represent the number of patients. AS: active surveillance; PI-RADS: Prostate Imaging-Reporting & Data System v2.1.

Biopsy results

Table 2 presents the pathologic results according to AS categories. Targeted-csPC, combined-csPC, and any cancer were identified in 182 (30%), 211 (35%), 383 (63%) patients, respectively. The targeted-csPC detection rate among AS patients (32%, 50 patients) was not different from the rate among non-AS patients (30%, 132 patients). AS was also not associated with the rates of targeted-csPC for each PI-RADS score. Any cancer and insignificant cancer detection rates were higher among the AS group, 74% and 38%, compared to 60% and 25% in the non-AS group, respectively (p<0.001 and p=0.002). AS was not associated with detection of targeted-csPC on univariate logistic regression analysis (OR 1.08, 95% CI 0.7–1.6, p=0.67).

Among the AS group, systematic biopsies upgraded the csPC detection rate of the targeted biopsies in 4% of patients; however, it was not statistically significant (p=0.47). Among the non-AS group, systematic biopsies upgraded the csPC detection rates of the targeted biopsies in 5% of patients, with a higher statistical significance (p=0.13).

Table 2. Comparison of biopsy results between AS categories

Characteristic	AS group (n=158)	Non-AS group (n=442)	p
Targeted-csPC	50 (32%)	132 (30%)	0.68
From PI-RADS 3 From PI-RADS 4 From PI-RADS 5	3/37 (8%) 28/91 (31%) 19/30 (63%)	7/111 (6%) 65/242 (27%) 60/89 (67%)	0.71 0.49 0.82
Combined-csPC	57 (36%)	154 (35%)	0.77
Any cancer	117 (74%)	264 (60%)	**<0.001**
Insignificant cancer	60 (38%)	110 (25%)	**0.002**

The categorical variables are reported as numbers (%). Bold indicates significant. AS: active surveillance; csPC: clinically significant prostate cancer; PI-RADS: Prostate Imaging-Reporting & Data System.

DISCUSSION

mpMRI is being extensively used both in targeting prostate biopsies for local tumor staging and in AS protocols for triggering biopsy performance. In this study, we evaluated 600 consecutive patients with suspicious PI-RADS 3–5 lesions on mpMRI who underwent combined prostate biopsies. We compared outcomes between patients under AS and those not on AS. Interestingly, the distribution of PI-RADS scores and their histologic outcomes were similar between the groups, and combined biopsies did not yield significantly higher rates of csPC compared to targeted biopsies alone in AS patients. Additionally, patients in the AS group were more frequently diagnosed with insignificant prostate cancer. Being on an AS protocol was not found to be a predictor of either higher PI-RADS scores or csPC detection on targeted biopsy.

Previous studies investigating PI-RADS scores for suspicious lesions on mpMRI have found a relatively consistent distribution across various prostate biopsy populations, with approximately 20–30% of lesions rated as PI-RADS 3, 40–50% as PI-RADS 4, and 20–30% as PI-RADS 5.[12-15] Additionally, the identification rates of csPC in patients undergoing biopsies were approximately 10–15% for PI-RADS 3, 20–30% for PI-RADS 4, and 60–80% for PI-RADS 5.[12,16] Our study found that the distribution of PI-RADS 3-5 scores and the targeted-csPC detection rates in the AS group were comparable to those in non-AS patients and aligned with the established literature. This suggests that mpMRI-detected suspicious lesions in patients under AS protocols are reliable for identifying csPC. Furthermore, as expected among patients already known to harbor PCa, a higher rate of insignificant PCa was detected in the AS group.

The roles of systematic, targeted, and combined biopsies have been extensively studied in prostate biopsy patients, with combined biopsies generally being identified as the most effective approach. In the study by Gomez-Gomez et al, it was shown that patients on an AS protocol benefit from the use of combined biopsies, whereas biopsy-naive patients or those with previously negative biopsies did not see the same benefit.[17] Similarly, the PAIREDCAP study by Elkhoury et al evaluated the value of adding targeted biopsies to systematic biopsies in biopsy-naive patients, concluding that combination biopsies provided the highest sensitivity for detecting csPC.[18] More recent findings suggest that in men with higher PSA density and PI-RADS scores, it may be safe to omit systematic biopsies in favor of targeted biopsies alone.[18]

Our study supports the idea that targeted biopsies may be sufficient for detecting csPC in AS patients with suspicious PI-RADS 3–5 lesions, as the addition of systematic biopsies did not result in a statistically significant improvement. Although we observed no difference in csPC detection rates between combined and targeted biopsies among non-AS patients, there is substantial evidence supporting the superiority of combined biopsies among biopsy-naive patients. For instance, Ahdoot et al found that in patients who underwent combined vs. targeted biopsies followed by radical prostatectomy, the rate of upgrades to ISUP 3 or higher was significantly lower with combined biopsies.[19]

Limitations

Our study has several inherent limitations. First, the retrospective design inherently limits its statistical power. We attempted to mitigate this by including consecutive patients in our analysis. Second, patients with negative MRI scans (PI-RADS 1–2) who underwent only systematic biopsies were not included. Third, we lacked precise data on the duration of AS and the timing of mpMRI within the AS protocol. Lastly, although our findings suggest that adding systematic biopsies to targeted biopsies did not significantly improve the detection rate of csPC in patients with suspicious PI-RADS 3–5 lesions, it might be underpowered for this purpose, and further prospective studies are needed to validate these results.

CONCLUSIONS

Our study demonstrates that mpMRI suspicious PI-RADS 3–5 lesions are reliable for the diagnosis of csPC during AS protocol. While the addition of systematic biopsies to targeted biopsies did not improve

csPC detection in AS patients with suspicious lesions, our findings suggest that targeted biopsies alone may be sufficient in this population; however, given the inherent limitations of our study, further prospective research is needed to confirm these findings and refine biopsy strategies in AS protocols. This could potentially lead to more tailored approaches, reducing unnecessary procedures while ensuring the detection of clinically significant disease.

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