Prostate International 9 (2021) 6–11

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international

Research Article

The significance of the visible tumor on preoperative magnetic resonance imaging in localized prostate cancer

Teak Jun Shin [a], Wonho Jung [a], Ji Yong Ha [a], Byung Hoon Kim [a,*], Young Hwan Kim [b]

[a] Department of Urology, Keimyung University School of Medicine, Dongsan Hospital, Daegu, Korea
[b] Department of Radiology, Keimyung University School of Medicine, Dongsan Hospital, Daegu, Korea

ARTICLE INFO

Article history:
Received 25 February 2020
Received in revised form
2 June 2020
Accepted 14 June 2020
Available online 26 June 2020

Keywords:
Biochemical recurrence
Localized prostate cancer
Magnetic resonance imaging
Visible tumors

ABSTRACT

Objectives: We investigated the relationship between tumor characteristics and visible tumors on magnetic resonance imaging (MRI) and examined the prognosis of tumor detection on MRI compared with no tumor detection in localized prostate cancer.

Materials and methods: We reviewed 214 patients with pT2N0M0 prostate cancer who underwent radical prostatectomy between January 2009 and December 2016. All the patients underwent MRI preoperatively. The patients were divided into 2 groups postoperatively: no visible tumor on the MRI group ($n = 96$, 44.9%) and visible tumor on the MRI group ($n = 118$, 55.1%). The visible tumor was defined as Prostate Imaging Reporting and Data System, version 2 Grade $\geq$ 3 on MRI. Age, prostate-specific antigen, prostate volume, positive surgical margin (PSM), lymphovascular invasion, and biochemical recurrence (BCR) were compared between the 2 groups. We also assessed the relationship between visible tumors on MRI and oncologic characteristics.

Results: The visible tumor on the MRI group showed a higher Gleason score $\geq 4 + 3$ [45.8% versus (vs.) 17.7%], high frequency of postoperative PSMs (28.8% vs. 16.7%), and higher BCR rate (17.8% vs. 7.3%) than the no visible tumor on the MRI group. The Kaplan–Meier analysis for BCR-free survival also showed a significant difference ($P = 0.006$). In multivariate Cox regression analysis, the detection of tumors on MRI was associated with a higher BCR risk [hazard ratio: 3.35; 95% confidence interval (CI): 1.36-8.27; $P = 0.009$]. We found a positive association between visible tumors on MRI and primary Gleason pattern of $\geq$4 (odds ratio: 4.31; 95% CI: 2.21–8.40; $P < 0.001$).

Conclusions: In localized prostate cancer, BCR was significantly more frequent when the tumor was detected on MRI, and a visible tumor on MRI was associated with the Gleason score. Therefore, attention should be paid to the possibility of high-grade prostate cancer when a tumor is detected on MRI before radical prostatectomy, and active follow-up may be needed postoperatively.

1. Introduction

Globally, prostate cancer is the most common cancer in men, and its incidence is increasing [1, 2]. The dissemination of prostate-specific antigen (PSA) tests has led to the discovery of many localized prostate cancers, and there have been many advances in treatment of such cancers [3]. Correct preoperative tumor staging in localized prostate cancer is necessary to predict the prognosis and to determine the appropriate treatment methods [4, 5]. However, PSA levels, results of the digital rectal examination, pathologic findings from biopsy, and transrectal ultrasonography have been limited in predicting preoperative tumor staging [6, 7]. To compensate for this, magnetic resonance imaging (MRI) examination has recently been selectively recommended [8]. MRI is characterized by no radiation exposure, and it has more advantages in obtaining information about the location, sized, and aggressiveness of the tumor [9-11]. Recently, many studies of prostate cancer and MRI have been published. In particular, several studies have been conducted to predict the stage of T2 and T3 tumors, one of the important prognostic factors determined by MRI [12,13]. As a result, concerns about positive surgical margins (PSMs) can be reduced, and the tumor stage can be helpful in determining treatment methods, such as the preserving neurovascular bundle during surgery.

* Corresponding author. Department of Urology, Keimyung University School of Medicine, Dongsan Hospital, 1035 Dalgubeoldae-ro, Dalseo-gu, Daegu, 42601, Korea.
E-mail address: blackporori@dsmc.or.kr (B.H. Kim).

https://doi.org/10.1016/j.prnil.2020.06.001

Although prostate cancer has been diagnosed by histological examination, tumors are not always identified by MRI. Therefore, we investigated the relationship between tumor characteristics and visible tumors on MRI and examined the prognosis of tumor detection on MRI compared with no tumor detection in localized prostate cancer. We hypothesized that prostate cancer, which is not radiologically visible, has a small tumor size and low Gleason score, and therefore, the presence of visible tumor on MRI may be an important predictor of the patient's prognosis.

2. Materials and Methods

2.1. Study participants

From January 2009 to December 2016, we retrospectively reviewed the medical records of patients who were diagnosed with prostate cancer and underwent radical prostatectomy after obtaining approval of Institutional Review Board (IRB 2020-01-017). The participants were 214 patients with pathological stage T2N0M0 who underwent MRI preoperatively. The patients were divided into 2 groups postoperatively: no visible tumor on the MRI group ($n = 96$, 44.9%) and visible tumor on the MRI group ($n = 118$, 55.1%). In these groups, age at operation, preoperative PSA, prostate volume, preoperative PSA density (PSAD), postoperative pathological Gleason score, postoperative pathological tumor volume, the presence of PSMs, lymphovascular invasion (LVI), and biochemical recurrence (BCR) were analyzed. In addition, we investigated the relationship between the patients with prostate cancer whose tumors were identified on preoperative MRI and the oncological characteristics of the prostate cancer (preoperative PSAD, pathological tumor volume, and postoperative pathological Gleason score). Furthermore, only the patients who had negative surgical margins in the entire participant group were divided into the no visible tumor and visible tumor on the MRI group, and the above factors were compared. Finally, the factors were compared in only the patients with a low-risk prostate cancer (PSA level $\leq$10 ng/mL, Gleason score $\leq$6).

2.2. Tumor detection by MRI

All patients underwent prostate biopsy using transrectal ultrasonography and then MRI at least 3 weeks after the biopsy. The 3 Tesla multiparametric MRI scanner (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) was used. One radiologist with 5 years of urological imaging experience reviewed the MRI findings via T2-weighted imaging and diffusion-weighted imaging including apparent diffusion coefficient and dynamic contrast-enhanced MRI. Clinical results of the participants were unknown and interpreted using the Prostate Imaging Reporting and Data System (PI-RADS), version 2.0. PI-RADS used a 5-point scale based on the probability of developing clinically significant prostate cancer [14]. On the 5-points scale, 1 point was very low (clinically significant cancer highly unlikely), 2 points was low (clinically significant cancer unlikely), 3 points was intermediate (clinically significant cancer equivocal), 4 points was high (clinically significant cancer likely), and 5 points was very high (clinically significant cancer highly likely), and we defined a PI-RADS score $\geq$3 as a visible tumor on preoperative MRI.

2.3. Statistical analysis

The clinical and pathologic factors and prognostic differences between the no visible tumor on MRI and visible tumor on MRI groups on preoperative MRI were compared by using the independent t-test, one-way analysis of variance, and Pearson chi-square test. Logistic regression analysis was used to evaluate the association between visible tumors on MRI, preoperative PSAD, postoperative pathological tumor volume, and Gleason score. Kaplan–Meier analysis and the log-rank test were used to compare the BCR-free survival for the postoperative pathological Gleason score, presence of PSMs, and visible tumors on MRI. In addition, Cox regression analysis was used to investigate the independent effects of each factor on BCR. The statistical program used was SPSS, version 21.0 (IBM Corp., Armonk, NY, USA), and data were considered statistically significant when the *P*-value was <0.05.

3. Results

Table 1 shows the results of comparing the characteristics between the no visible tumor on the MRI group and visible tumor on MRI group. There was no significant difference in age, PSA, prostate volume, PSAD, tumor volume, and LVI. However, the visible tumor on the MRI group had a higher Gleason score ($P < 0.001$) and higher frequency of PSMs ($P = 0.037$) than the no visible tumor on MRI group. Fifty three (44.9%) patients in the visible tumor on the MRI group and 15 (15.6%) in the no visible tumor on the MRI group had a first Gleason pattern of $\geq$4, which was significantly different ($P < 0.001$). During the median 48.8-month follow-up period, BCR was present in 28 of the total patients (13.1%): 7 patients (7.3%) in the no visible tumor on the MRI group and 21 patients (17.8%) in the visible tumor on the MRI group. The probability of developing BCR was significantly higher when tumors were identified on MRI ($P = 0.023$).

In logistic regression analysis, there was no significant correlation between visible tumor on preoperative MRI, PSAD, and tumor volume. However, when a tumor was identified by MRI, there was a significant correlation with the first Gleason pattern of $\geq$4 [odds ratio: 4.31; 95% confidence interval (CI): 2.21–8.40; $P < 0.001$] (Table 2).

BCR-free survival was analyzed by Kaplan–Meier curves for the Gleason score, PSM, and visible tumor on MRI, which showed significant differences in the results of Table 1 (Fig. 1). BCR-free survival was significantly lower in patients with a high Gleason score ($P = 0.029$), PSM ($P = 0.002$), and visible tumor on MRI ($P = 0.006$). In multivariate analysis, PSM [hazard ratio (HR): 2.76; 95% CI: 1.27–6.00; $P = 0.010$], LVI (HR: 4.29; 95% CI: 1.52-12.11; $P = 0.006$), and visible tumor on MRI (HR: 3.35; 95% CI: 1.36–8.27; $P = 0.009$) were identified as significant predictors of BCR (Table 3).

To analyze the prediction of BCR in accordance with MRI findings, we divided 164 patients (76.6%), except for those with PSMs, into 2 groups of no visible tumor and visible tumor on MRI (Table 4). Among them, 80 patients (48.8%) had no visible tumor on MRI, and 84 patients (51.2%) had a visible tumor on MRI. The visible tumor on MRI group had a lower prostate volume ($P = 0.041$), higher PSAD ($P = 0.034$), and higher Gleason score ($P < 0.001$) than the no visible tumor on MRI group. During the median 49.7-month follow-up, BCR was significantly different between the groups, despite the exception of patients with PSMs (no visible tumor group: 5.0% versus visible tumor group: 14.3%; $P = 0.039$).

The no visible tumor and visible tumor on the MRI group were compared in terms of low-risk prostate cancer (Table 5). Twenty nine patients (13.6%) had low-risk prostate cancer. Among them, 20 patents (69.0%) had no visible tumor on MRI, and 9 patients (31.0%) had visible tumors on MRI. There was no significant difference in clinical and pathologic characteristics between the groups. BCR did not occur in the no visible tumor on MRI group, but BCR occurred in 3 patients (33.3%) of the visible tumor on the MRI group during the median 64.6-month follow-up ($P = 0.023$).

Table 1
Characteristics between no visible tumor and visible tumor on magnetic resonance imaging in localized prostate cancer.

Characteristics	No visible tumor on MRI (n = 96)	Visible tumor on MRI (n = 118)	*P*-value
Age (years)	66.0 (±6.7)	67.4 (±6.2)	0.110
PSA (ng/mL)	8.0 (±10.1)	9.2 (±12.1)	0.413
PV (cc)	43.2 (±19.7)	39.1 (±18.8)	0.128
PSAD (ng/ml/cc)	0.22 (±0.25)	0.26 (±0.24)	0.290
Gleason score			<0.001
6	24 (25.0%)	12 (10.2%)	
7 (3 + 4)	55 (57.3%)	52 (44.1%)	
7 (4 + 3)	9 (9.4%)	37 (31.4%)	
8–10	8 (8.3%)	17 (14.4%)	
Tumor volume (cc)	3.1 (±5.5)	3.8 (±3.8)	0.263
PSM	16 (16.7%)	34 (28.8%)	0.037
LVI	6 (6.3%)	8 (6.8%)	0.876
BCR	7 (7.3%)	21 (17.8%)	0.023

MRI, magnetic resonance imaging; PSA, prostate-specific antigen; PV, prostate volume; PSAD, PSA density; PSM, positive surgical margin; LVI, lymphovascular invasion; BCR, biochemical recurrence.

4. Discussion

MRI is important in staging, surgical planning, and treatment of prostate cancer [5, 15-19]. In clinical practice, MRI is commonly used when prostate cancer is diagnosed with an increased PSA level. However, tumors are often not identified on MRI of patients diagnosed with prostate cancer [15,19], and the accuracy and false negative rate of detecting prostate cancer on MRI are still controversial.

No studies have reported the significance of MRI in postoperative pathologic stage T2N0M0 prostate cancer. The strength of this study is that it confirmed the characteristics and significance of tumor detection by MRI regardless of the degree of invasion and stage. Further, the accurate Gleason scores confirmed the association with visible tumors on MRI because the pathologic results of the entire prostate specimens after radical prostatectomy were used, not the pathological results of the needle biopsy.

Previous studies have found that tumors with a low density of cancer cells were similar to normal prostate findings on MRI compared with tumors with a high density [20]. There have also been reports that low intensity on MRI is associated with high Gleason scores [21, 22], and recent studies have shown that higher Gleason scores increased the accuracy of tumor detection by MRI [23]. Two other studies reported that the sensitivity of detecting prostate cancer on MRI was related to tumor size, as well as the Gleason score [18, 24]. Our study also confirmed that tumors identified on MRI were associated with high Gleason scores. However, detection was not related to the tumor size, and only the Gleason score correlated with visible tumors on MRI. Especially, the first Gleason pattern of $\geq$4 showed a significant association. This finding indicates that tumors can be identified on MRI when there is a large distribution of prostate cancer tissue with poor differentiation, regardless of the tumor size. In addition, the visible tumors on preoperative MRI indicate that physicians may consider aggressive treatment with the potential for clinically significant prostate cancer with Gleason scores of 4 + 3 or higher.

Here, patients with visible tumors on preoperative MRI had higher PSMs and increased risk of BCR compared with patients with no visible tumors. In the Kaplan–Meier analysis of BCR-free survival, the visible tumor on MRI group showed similar graphs as no visible tumor on the MRI group in terms of a high Gleason score and PSMs. In multivariate Cox regression analysis, visible tumors on preoperative MRI were independent indicators for predicting BCR, and the risk of BCR was 3.35 times higher in the visible tumor on the MRI group than in the no visible tumor on MRI.

In clinical practice, PSM is already known as a factor affecting BCR [25], and our results confirm that PSM was a significant predictor of BCR. Because the surgeon's technique may affect the postoperative oncological outcome, we analyzed the patient group without considering PSM. In patients with a negative PSM, a higher occurrence of BCR was found when MRI confirmed the visible tumor. These results suggest that the presence of tumors detected by preoperative MRI in patients with local prostate cancer is likely to predict postoperative BCR.

Studies have shown that the higher stage determined by preoperative MRI, the higher risk of BCR [12, 13]. In contrast, few studies have analyzed the relationship of BCR with or without tumor detection by MRI. A study of 158 patients with prostate cancer who underwent radical prostatectomy suggested that low apparent diffusion coefficient values in diffusion-weighted imaging MRI could be an important predictor of postoperative BCR [26]. In a recent study of 282 patients with prostate cancer who underwent radical prostatectomy (median follow-up 26 months), the presence of visible tumors on preoperative 3 Tesla multiparametric MRI was the only independent factor for predicting postoperative BCR [27]. Those reported results are similar to the present study's findings. However, unlike our study, those studies included prostate cancer of stage T3 or higher, and multivariate analysis did not include pathological characteristics, such as postoperative staging.

Some studies have shown that tumors detected by MRI were not associated with prognosis. A study of 92 patients with prostate cancer who chose active surveillance reported that visible tumors on MRI were not associated with BCR [28]. However, this study included a small number of patients and lacked criteria for active surveillance, which included prostate cancer at various grades and stages. In contrast, another study comparing patients who satisfied the inclusion criteria for active surveillance and those with low-risk prostate cancer who did not meet the active surveillance

Table 2
Multivariate logistic regression analysis for visible tumor on magnetic resonance imaging in localized prostate cancer.

Characteristics	OR (95% CI)	*P*-value
PSAD[a)]	1.12 (0.32–3.99)	0.860
Tumor volume[b)]	1.03 (0.96–1.109)	0.410
Primary Gleason pattern $\geq$ 4	4.31 (2.21–8.40)	<0.001

OR, odd ratio; CI, confidence interval; PSAD, prostate-specific antigen density.
[a)] ORs are for every 0.01 ng/mL/cc in PSAD.
[b)] ORs are for every 0.1 cc in tumor volume.

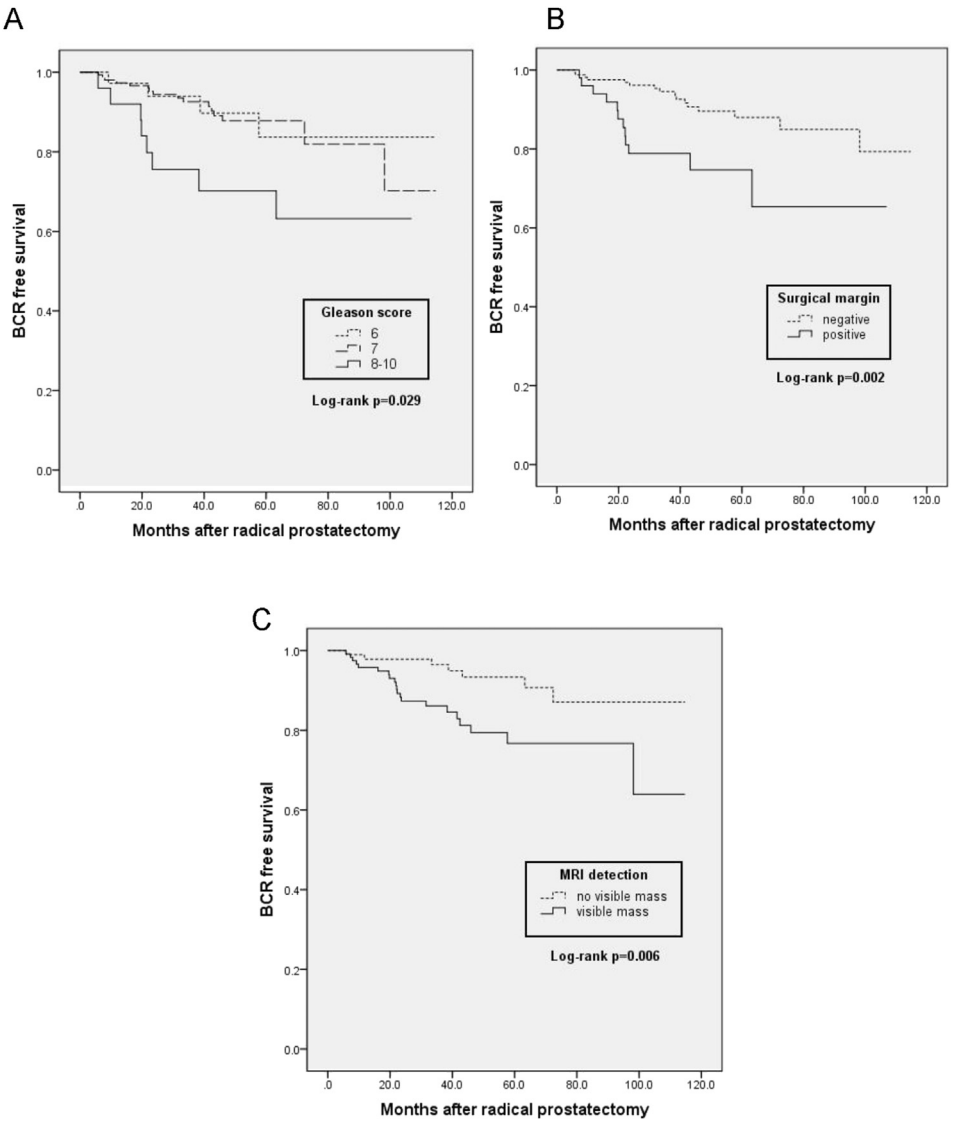

Fig. 1. Kaplan–Meier survival analysis for biochemical recurrence free survival in localized prostate cancer. (A) Gleason score. (B) Surgical margin status. (C) Tumor detection on magnetic resonance imaging. BCR, biochemical recurrence; MRI, magnetic resonance imaging.

criteria showed similar pathological results in cases where visible tumors were not identified on MRI [29]. They also reported that in patients with low-risk prostate cancer at the clinical stage, visible tumors on MRI showed more intermediate or high-risk pathological outcomes after prostatectomy. This finding means that in patients with low-risk prostate cancer, those with no visible tumor on MRI may be offered active surveillance, whereas those with visible tumors on MRI may be offered active treatment. Here, 29 patients with low-risk prostate cancer were divided into those with visible tumors and those without visible tumors on preoperative MRI, and 66.7% of patients in the visible tumor on the MRI group showed BCR-free survival during the 5-year follow-up period. This result was a low survival rate compared with that in a study that reported a 5-year BCR-free survival rate of proximately 85% among patients with low-risk prostate cancer who underwent radical prostatectomy [30]. Although studies involving a larger number of patients will be needed, it is important to consider that visible tumors on MRI are more likely to result in BCR than invisible tumors on MRI even in low-risk prostate cancer.

Our research study has some limitations. First, this study had a retrospective, single-institution design, and included a small number of patients. It is possible that there was selective bias in our

Table 3
Multivariate Cox regression analysis for biochemical recurrence in patients with localized prostate cancer.

Characteristics	HR (95% CI)	*P*-value
Age	1.01 (0.95-1.08)	0.678
PSA	1.01 (0.98-1.03)	0.569
PV	1.00 (0.98-1.02)	0.978
Gleason score[a)]	1.17 (0.54-2.54)	0.699
Tumor volume	0.97 (0.87-1.09)	0.616
PSM	2.76 (1.27-6.00)	0.010
LVI	4.29 (1.52-12.11)	0.006
Visible tumor on MRI	3.35 (1.36-8.27)	0.009

HR, hazard ratio; CI, confidence interval; PSA, prostate-specific antigen; PV, prostate volume; PSM, positive surgical margin; LVI, lymphovascular invasion; MRI, magnetic resonance imaging.
[a)] HRs are for every 1 in Gleason score.

Table 4
Characteristics between no visible tumor and visible tumor on magnetic resonance imaging in localized prostate cancer excluding positive surgical margin patients.

Characteristics	No visible tumor on MRI (n = 80)	Visible tumor on MRI (n = 84)	*P*-value
Age (years)	65.8 (±6.5)	67.3 (±6.3)	0.136
PSA (ng/mL)	7.1 (±4.7)	9.5 (±13.8)	0.142
PV (cc)	45.6 (±20.1)	39.2 (±19.6)	0.041
PSAD (ng/ml/cc)	0.19 (±0.15)	0.26 (±0.27)	0.034
Gleason score			<0.001
6	23 (28.8%)	12 (14.3%)	
7 (3 + 4)	45 (56.3%)	32 (38.1%)	
7 (4 + 3)	8 (10.0%)	28 (33.3%)	
8–10	4 (5.0%)	12 (14.3%)	
Tumor volume (cc)	2.4 (±3.0)	3.4 (±3.6)	0.066
LVI	4 (5.0%)	6 (7.1%)	0.404
BCR	4 (5.0%)	12 (14.3%)	0.039

MRI, magnetic resonance imaging; PSA, prostate-specific antigen; PV, prostate volume; PSAD, PSA density; LVI, lymphovascular invasion; BCR, biochemical recurrence.

Table 5
Characteristics between no visible tumor and visible tumor on magnetic resonance imaging in low-risk prostate cancer.

Characteristics	No visible tumor on MRI (n = 20)	Visible tumor on MRI (n = 9)	*P*-value
Age (years)	64.3 (±7.1)	67.2 (±7.0)	0.311
PSA (ng/mL)	5.4 (±2.2)	5.9 (±1.7)	0.591
PV (cc)	49.2 (±25.5)	45.6 (±26.1)	0.731
PSAD (ng/ml/cc)	0.13 (±0.09)	0.15 (±0.07)	0.603
Tumor volume (cc)	1.2 (±2.2)	1.8 (±1.5)	0.483
PSM	1 (5.0%)	0	0.690
LVI	0	0	
BCR	0	3 (33.3%)	0.023

MRI, magnetic resonance imaging; PSA, prostate-specific antigen; PSAD, PSA density; PSM, positive surgical margin; LVI, lymphovascular invasion; BCR, biochemical recurrence.

study design. Second, data were interpreted using PI-RADS, version 2 on MRI, but it is possible that the subjective views of the diagnostic radiologist were included. Although the interpretation was done by an experienced radiologist, it is also possible that one person interpreted the MRI findings and that there was bias in that interpretation.

When tumors were identified by preoperative MRI in localized prostate cancer, they were associated with a higher grade of cancer, and the possibility of BCR was high. Therefore, if tumors are detected on preoperative MRI, treatment should be decided with the possibility of clinically significant prostate cancer, and even in low-risk prostate cancer, active follow-up may be necessary in consideration of the higher possibility of BCR.

Conflicts of interest

None declared.

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