Sensitivity of prostate cancer foci using 1.5 T multiparametric magnetic resonance imaging

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Research article

Abstract

Background

The detection of prostate cancer (CaP) has increasingly being carried out by multiparametric magnetic resonance imaging (mpMRI). Despite many previous studies, the sensitivity for clinically significant CaP (csCaP) was high, information on mpMRI false-negative lesions is limited. Therefore, the aim of this study was to evaluate the use and limitations of mpMRI in CaP.

Methods

A total of 228 CaP foci in 100 patients who underwent 1.5 T mpMRI and radical prostatectomy between December 2015 and June 2017 were retrospectively analyzed. The sensitivities of CaP foci, csCaP, and index tumors (ITs) were measured. Clinically significant CaP was defined into two categories based on the Gleason score (GS): csCaP/GS ≥ 3 + 4 (GS ≥ 3 + 4 or diameter > 10 mm) and csCaP/GS ≥ 4 + 3 (GS ≥ 4 + 3 or diameter > 10 mm). In addition, the characteristics of false-negative lesions were identified. The Prostate Imaging Reporting and Data System version 2 was used to determine an mpMRI positive lesion, defined as a lesion having a score of ≥ 3.

Results

The sensitivity of all legions, csCaP/GS ≥ 3 + 4, csCaP/GS ≥ 4 + 3, and ITs were 61.4%, 75.8%, 83.0%, and 91%, respectively. There were 91 lesions that were mpMRI false, 40% of which were csCaP/GS ≥ 3 + 4. There were three lesions with a GS of ≥ 8 and ≥ 10 mm in the false-negative results.

Conclusions

mpMRI can highly detect ITs and csCaP/GS ≥ 4 + 3; however, a few large and high-GS CaPs constitute undetectable lesions in 1.5 T mpMRI.

Background

Prostate cancer (CaP) is the second most prevalent cancer and fifth common cause of cancer death among men worldwide[1]. Currently, CaP is diagnosed using prostate-specific antigen level, digital rectal examination, and transrectal ultrasound-guided systemic biopsy as a standard care. However, overdiagnosis of insignificant CaP and misdiagnosis of clinically significant cancer (csCaP) can result from these strategies.

In recent years, after the emergence of multiparametric magnetic resonance imaging (mpMRI), the use of MRI in CaP has increased considerably. Previously, the capability of prostate MRI, which was assessed

using T1- and T2-weighted imaging (T2WI), to detect CaP was limited. However, there have been improvements in the detection of CaP through multiparametric MRI, which combines anatomic T2WI with functional and physiologic assessment, including diffusion-weighted imaging (DWI) and its derivative, apparent-diffusion coefficient, dynamic contrast-enhanced (DCE) MRI, and, sometimes, other techniques such as *in vivo* magnetic resonance proton spectroscopy[2–16]. However, information on mpMRI false-negative lesions in previous reports is limited, and in most of these studies, 3 T mpMRI was used. Nevertheless, 1.5 T MRI was still used.

Therefore, we aimed to analyze the sensitivities of 1.5 T mpMRI without endorectal coil using radical prostatectomy (RP) specimens. In particular, we examined the details of false-negative lesions.

Patients And Methods

Patients

Men who underwent RP in Yamagata University Hospital between December 2015 and June 2017 were included in this study. Patients who received androgen deprivation therapy and transurethral resection of prostate before surgery were excluded.

mpMRI

All patients underwent 1.5 T mpMRI without endorectal coil before prostate biopsy. The orientation of the DWI and DCE MRI was the same as for the T2WI. Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) was used to evaluate the images obtained and were scored as follows: 1, clinically significant disease highly unlikely to be present; 2, clinically significant cancer unlikely to be present; 3, the presence of clinically significant cancer is equivocal; 4, clinically significant cancer likely to be present; and 5, clinically significant cancer highly likely to be present[17]. Basically, an mpMRI positive lesion was defined as a lesion with a score of ≥3 in the PI-RADS v2.

Pathological analysis

Whole prostate specimens were fixed in 10% buffered formaldehyde for 48 h, after which the specimens were sectioned perpendicular to the urethra in 4–6-mm serial axial slices and embedded into paraffin (FFPE block). A 5-μm-thick FFPE section was mounted on glass slides and stained with hematoxylin and eosin.

Each major cancer foci was evaluated for Gleason score (GS), largest size (mm), extra-prostatic extension (EPE), and surgical margin (SM). For each patient, up to three foci were always evaluated, but beyond that, minimal lesions were excluded.

IT was defined as a lesion having a maximum foci or a high GS within 5 mm of the maximum, which is considered to reflect mainly the prognosis[18, 19]. Prostate cancer was categorized into two groups:

csCaP/GS ≥3 + 4 (GS ≥3 + 4 or diameter >10 mm) and csCaP/GS ≥4 + 3 (GS ≥4 + 3 or diameter >10 mm).

Statistical analyses

Differences were compared using the Welch *t* test and the Fisher test, and the free statistical software package R version 3.5.2 (https://cran.r-project.org) was used to perform all statistical analyses.

Results

Clinicopathological characteristics

The characteristics of the 100 patients who underwent mpMRI before prostate biopsy and RP (96 robot-assisted and 4 open) are shown in Table 1. The following characteristics were found for the patients (median [range]): age, 67 years (52–78 years); prostate-specific antigen level, 7.14 ng/ml (3.33–28.24 ng/ml); and prostate volume, 36.0 g (19.5–74.0 g). According to National Comprehensive Cancer Network guidelines, of the 100 patients, 11, 60, and 29 were classified into low, intermediate, and poor risk, respectively.

Data on a total of 228 tumor foci that were detected in tumors in the 100 RP specimens are shown in Table 2. GS was 6 in 94 (41.2%), 3 + 4 in 72 (31.5%), 4 + 3 in 27 (11.8%), and ≥8 in 35 (15.4%) specimens. As for tumor location, 153 (67.1%) and 75 (32.8%) tumors were located in the peripheral and transition zones, respectively. Moreover, positive rates of EPE and SM were higher in IT (*n* = 100) than in non-IT (*n* = 128) (*p* < 0.001) (Table 2).

Sensitivity of mpMRI

The sensitivity of all 228 lesions was 61.4%. The ITs, csCaP/GS ≥4 + 3, diameter >10 mm, and GS ≥8 had relatively high sensitivities (91.0%, 85.3%, 85.7%, and 85.7%, respectively). There lesions with a diameter <10 mm, especially in the specimens with low GS had low sensitivities (diameter <10 mm, diameter <10 mm and GS 6, diameter <10 mm, and GS 3 + 4 had sensitivities of 31.1%, 24.6%, and 31.6%, respectively). Although lesions with a GS of 6 had low sensitivities (36.1%), lesions with a diameter of ≥10 mm were highly detected even in GS 6 (76.2%). Positive EPE and positive SM had relatively high sensitivities as well (91.7% and 79.2%, respectively). Approximately half of the lesions (48.2%) was mpMRI positive lesion. Whereas 72.2% of the lesions with a diameter >10 mm were diagnosed, only 22.0% of the lesions with a diameter of ≤10 mm were diagnosed (Table 3).

Characteristics of mpMRI false-negative lesions

There were 91 (39.9%) mpMRI false-negative lesions, 58 and 33 of which were classified as PI-RADS score 1 and 2, respectively. Surprisingly, 40.7% of mpMRI false-negative lesions were csCaP/GS ≥3 + 4, and 51.5% of score 2 lesions were csCaP/GS ≥4 + 3. Although only five lesions (5.5%) were GS ≥8, three

of these had diameters ≥10 mm (Table 4). Of the nine mpMRI false-negative ITs, seven were GS ≤3 + 4; however, two lesions were large and GS 4 + 5 (Table 5).

Sensitivity of pT3

Lesions that were upgraded to pT3 are shown in Table 6. Only four (11.8%) cases of 13 pT3 were diagnosed as cT3 by mpMRI. On the other hand, all pT3 were diagnosed as cT3 by mpMRI.

Discussion

The overall results of this study are similar to those of previous studies. The sensitivity of all lesions with a PI-RADS score of ≥3 was 61.4% in this study and 31%–62% in previous studies that used RP specimens (Table 3)[6, 10, 15, 20]. The low sensitivity of all lesions reflects the low sensitivity of small and low-GS lesions. However, even in GS ≥8, mpMRI misdiagnosed one-third of the lesions with diameters of ≤10 mm. In lesions with GS 3 + 4 and diameter ≤10 mm, the sensitivity was only 31.6%, which caused the low sensitivity of csCaP/GS ≥3 + 4 (77.7%) (Table 3). Detection rates for csCaP/GS ≥3 + 4 (67%–75%) in previous studies were similar.

csCaP is usually defined as lesions with GS ≥3 + 4 or diameter >10 mm[21]. However, National Comprehensive Cancer Network guidelines also recommend active surveillance for GS 3 + 4 lesions. In addition, some recent studies have defined GS ≥4 + 3 as csCaP[8]. Therefore, we used two types in the analysis of csCaP. Compared with csCaP/GS ≥3 + 4, the sensitivity of csCaP/GS ≥4 + 3 in this study (85.7%) and in previous studies (91%–95%) was relatively high[8] [22] (Table 3).

It has been suggested in recent reports that lesions associated with cancer progression and metastasis could be the largest lesions in prostate or highest GS within 5 mm of maximum, called IT[18] [19]. Focal therapy for limited CaP is rationally based on IT hypothesis. Multiparametric MRI, which might be considered a suitable tool for IT detection, has a high detection rate for IT (91% in this study and 80%–91% in the previous studies). Nevertheless, the approximately 10% rate of misdiagnosis needs our attention (Table 3).

Tumors undetected in mpMRI are often characterized as small and multifocal[23]. Ninety-one (39.9%) lesions in this study were mpMRI negative, 67 (73.6%) of which were insignificant cancers (GS ≤3 + 4 and ≤10 mm) (Table 4). In case of IT, most undiagnosed lesions were multifocal cancers. However, it was surprising that two cases had an IT with ≥20 mm and GS 4 + 5. A previous study using mainly 3 T mpMRI mentioned that mpMRI negative lesions could be high GS, but large lesions with a high GS were fully detectable[4]. The intensity of the applied magnetic field may be reason for the missing cases with high-grade and large lesions in our study. In a study by Ulrich et al., the correlation between 1.5 and 3 T within the same patients was reported. This study revealed that comparable objective image quality is revealed by 1.5 T MRI in T2WI but is inferior to 3 T in DWI. The conclusions of the study indicated feasible diagnostic performance even in 1.5 T MRI[24]. However, the inferiority of 1.5 T MRI in DWI might lead to the misdiagnoses in this study.

Positive SM is an important factor that reflects the postoperative outcome[25] [26]. Postoperative functional outcomes, including continence and erectile function, are improved by neurovascular bundle preservation techniques[27] [28], which potentially increase positive SM when neurovascular bundle is preserved on the EPE positive side. Although mpMRI is mainly used to predict EPE before surgery, previous reports have mentioned that the sensitivity of EPE is not enough. A meta-analysis showed a sensitivity of 57% and a specificity of 91% for microscopic EPE[29]. The sensitivity and specificity in this study were only 11.8% and 100%, respectively (Table 6). Positive mpMRI lesions had more positive EPE and SM than mpMRI negative lesions (Table 3).

Several limitations of this study should be mentioned. First, this was a retrospective study. Second, the PI-RADS score was estimated by a single physician. Several studies have revealed that there are diagnostic differences across readers[10, 30]. Third, there could be differences in characteristics between patients who underwent RP in this study and those who underwent other treatments. Fourth, up to three lesions were always evaluated; however, minimal lesions beyond these three were excluded from this analysis.

Conclusions

Detection of IT and csCaP/GS ≥ 4 + 3 through mpMRI is high; however, large and high-GS CaPs are sometimes undetected in 1.5 T mpMRI.

Abbreviations

CaP; prostate cancer, csCaP; clinically significant prostate cancer, MRI; magnetic resonance imaging, mpMRI; multiparametric magnetic resonance imaging, T2WI; T2-weighted imaging, DWI; diffusion-weighted imaging, DCE; dynamic contrast-enhanced, RP; radical prostatectomy, PI-RADS v2; Prostate Imaging Reporting and Data System version 2, GS; Gleason score, EPE; extra-prostatic extension, SM; surgical margin.

Declarations

Ethics approval and consent to participate

The ethics committee of Yamagata University Faculty of Medicine approved the study (approval no.H28-34). The methods were conducted in accordance with the approved guidelines. All participates in this study have consented to participate with our institutional consent form.

Availability of data and materials

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

Authors' contributions

SI, SN, TK, and NT participated in the design of the present study. SI drafted the manuscript and figures. SI performed statistical analyses. TN, MY, YK, HK, AY, TS, HN, and TY collected data. SN, TK, and NT participated in the coordination and helped with the drafting of the manuscript. All authors have read and approved the final manuscript.

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