Research Article

The value of magnetic resonance imaging and ultrasonography (MRI/US)-fusion biopsy in clinically significant prostate cancer detection in patients with biopsy-naïve men according to PSA levels: A propensity score matching analysis

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Objectives: To evaluate the detection rate of clinically significant prostate cancer (csPCa) in Magnetic resonance imaging and ultrasonography (MRI/US) fusion biopsy in patients with biopsy-naïve men for varying prostate-specific antigen (PSA) levels. Since MRI can efficiently detect csPCa compared to standard transrectal ultrasound (TRUS) guided biopsy; however, the optimal PSA threshold for its use is unclear.

Materials and methods: We retrospectively reviewed those who underwent MRI/US-fusion and standard biopsy from January 2016 to June 2018. Patients were divided into three groups: PSA < 4, 4-10, >10 ng/mL. Propensity scoring was performed to balance the characteristics of the different biopsy groups, and the detection rate of csPCa was compared.

Results: Data from a total of 670 males were included in the analysis (standard TRUS, n = 333; MRI/US fusion, n = 337). Prior to matching, patients who received MRI/US-fusion biopsy had lower prostate volume. Propensity score matching balanced this characteristic and generated a cohort comprising 195 patients from each group. In the matched cohort, patients with PSA 4-10 ng/mL had a significantly increased risk of csPCa by MRI/US-fusion vs. standard biopsy (35.0% vs. 26.6%, P = 0.033). However, patients with PSA < 4 ng/mL had csPCa found by MRI/US-fusion versus standard biopsy (12.0% vs. 16.0%, P = 0.342), whereas, patients with PSA > 10 ng/mL had csPCa found by MRI/US-fusion versus standard biopsy (78.0% vs. 80.0%, P = 0.596). In multivariate logistic analysis among patients with PSA 4-10 ng/mL, MRI/US-fusion biopsy (odds ratio: 2.46, 95% confidence interval = 1.31-4.60, P = 0.005) were significantly associated with a detection of csPCa.

Conclusions: Detection of csPCa by MRI/US-fusion biopsy is more efficient in patients with biopsy-naïve men with PSA 4-10 ng/mL. However, standard TRUS biopsy may identify csPCa in patients with PSA < 4 ng/mL and > 10 ng/mL, emphasizing the importance of performing a standard biopsy in conjunction with MRI/US-fusion biopsy in such populations.

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targeted biopsies [3-6]. However, multiparametric MRI (mpMRI) is expensive and not commonly used in a clinical setting. Instead, a simplified biparametric MRI (bpMRI) protocol, comprising of only T2-weighted and diffusion-weighted imaging, has been proposed for the diagnosis of csPCa, [7, 8].

Therefore, we conducted MRI/US-fusion biopsy in patients with biopsy-naïve men with elevated PSA levels and compared the results of standard TRUS biopsy (TRUSbx), and we further compared the detection rate of csPCa in males with PSA in the gray zone in order to minimize overdiagnosis and unnecessary treatment.

2. materials and Methods

2.1. Study Subjects

We retrospectively reviewed the medical records of a total of 670 males that underwent either MRI/US-fusion (n = 337) biopsy or standard TRUSbx (n = 333) at the Keimyung University Dongsan Medical Center, from January 2016 to June 2018 (Fig. 1). The Institutional Review Board approved this study (DSMC 2020-11-033). We compared the following clinical variables: age (years), PSA (ng/mL), prostate volume (PV) (cc), Gleason score (GS, the greatest grade), clinical T stage, and lymph node metastasis and distant metastasis. All histopathological biopsies were reported (core length, cancer length, and GS) by a pathologist with at least 10 years of experience in genitourinary pathology. We defined csPCa with a GS 3+4 or greater [9]. The patients were then divided into three groups as follows; PSA <4 ng/mL, 4–10 ng/mL, and >10 ng/mL.

2.2. MRI protocol

The bpMRI examination was performed using a 3.0-T scanner with a 32-channel phased-array coil (Ingenia 3T CX Quasar Dual; Philips, The Netherlands). The Prostate Imaging Reporting and Data System version 2.1 (PI-RADSv2.1) scores were assigned by a radiologist (with at least 3 years of prostate MRI experience) on a scale from 1 to 5 [10]. In a case of a suspicious lesion on MRI (PI-RADS 3-5), a targeted biopsy (TBx) was conducted (from one to three cores) using the MRI-TRUS fusion software-assisted system (BioJET®, D&K Technologies, Barum, Germany) followed by six plus six systemic biopsy (SBx) cores [11]. All biopsies were performed by an experienced radiologist through a transrectal route with an enema and prophylactic antibiotics.

2.3. Statistical Analysis

The propensity score matching was performed to adjust for significant imbalances in baseline characteristics between two biopsy methods. This approach can be applied to minimize selection bias in observational data [12]. Categorical variables were compared between the groups using the chi-square, Fisher’s exact test, or linear-by-linear association, where appropriate. One-way analysis of variance or Student’s t-test was used for continuous variables. Binary logistic regression was used to estimate the odds of csPCa among males with PSA 4–10 ng/mL. The probability of csPCa was modeled by the stepwise regression of the following four predetermined potential risk factors. The 95% profile likelihood ratio confidence intervals (95% CIs) were calculated for the adjusted odds ratios (ORs). All statistical analyses were performed using SPSS version 25.0 software (IBM, Armonk, NY, USA). P-values less than 0.05 were considered to be statistically significant.

3. Results

3.1. Subjects Characteristics

A total of 670 males were included in the analysis (MRI/US fusion, n = 337; standard TRUS, n = 333) (Fig. 1). Among them, 348 (51.9%) were diagnosed with PCa, and 258 (38.5%) were diagnosed with csPCa. Details of descriptive statistics for the entire cohort (n = 670), as well as the propensity score-matched cohort (n = 390), are summarized in Table 1. In the entire cohort, there was a significant imbalance in prostate volume between the two groups. Mean PV in the standard TRUSbx group was higher than that of the MRI/US-fusion biopsy group (50.2 vs. 45.0; P = 0.002). Propensity score matching resulted in a cohort of 195 patients in each group. In the matched cohorts, there were no between-group differences with respect to patient baseline characteristics.

![Fig. 1. Flowchart of inclusion criteria of the final patient cohort.](image-url)
3.2. Detection of csPCa Among Patients with PSA level

Table 2 shows the detection rate of PCa and csPCa in the entire and matched cohort. The overall detection rate of csPCa of MRI/US-fusion versus standard TRUSbx groups was no significantly different in the unmatched (39.8% vs. 37.2%, \( P = 0.502 \)) and matched cohort (43.0% vs. 38.9%, \( P = 0.163 \)). In the matched cohort, in males with PSA 4–10 ng/mL, the detection rate of csPCa in the MRI/US-fusion biopsy was higher compared to the standard biopsy group (35.0% vs. 26.6%, \( P = 0.033 \)). The detection rate of csPCa in the standard biopsy group was not statistically different compared to the MRI/US-fusion group in males with PSA <4 ng/mL (12.0% vs. 16.0%, \( P = 0.342 \)) and in males with PSA >10 ng/mL (78.0% vs. 80.0%, \( P = 0.596 \)) (Fig. 2).

Table 3 summarizes the results of univariate and multivariate analysis for the csPCa in males with PSA 4–10 ng/mL. In a multivariate analysis, older age (OR = 1.10, 95% CI = 1.06–1.15, \( P < 0.001 \)), smaller PV (OR = 0.96, 95% CI = 0.93–0.98, \( P < 0.001 \)), and MRI/US-fusion biopsy (OR = 2.46, 95% CI = 1.31–4.60, \( P = 0.005 \)) were significantly associated with csPCa.

3.3. Presence of Suspicious Lesions on bpMRI

Subgroup analyses were performed to identify the presence of suspicious lesions on bpMRI. Among subjects that underwent

| Characteristics                          | Standard TRUS (n = 333) | MRI-fusion (n = 337) | P-value | Standard TRUS (n = 195) | MRI-fusion (n = 195) | P-value |
|------------------------------------------|-------------------------|----------------------|---------|-------------------------|----------------------|---------|
| Mean age, yr (SD)                        | 68.5 (8.3)              | 67.9 (8.9)           | 0.339   | 68.2 (8.6)              | 68.1 (8.5)           | 0.899   |
| Mean PSA, ng/mL (SD)                     | 45.1 (31.5)             | 35.6 (15.0)          | 0.619   | 40.3 (24.6)             | 40.2 (20.7)          | 0.990   |
| Mean PV, cc (SD)                         | 50.2 (23.7)             | 45.0 (19.3)          | 0.002   | 47.6 (21.7)             | 47.5 (17.3)          | 0.946   |
| Mean total biopsy core, n                | 12.3 (1.4)              | 13.0 (2.1)           | <0.001  | 12.3 (1.3)              | 12.7 (1.6)           | 0.502   |
| PCA diagnosis, n (%)                     | 184 (55.3)              | 164 (48.7)           | 0.088   | 112 (57.4)              | 103 (52.8)           | 0.089   |
| Gleason score, n (%)                     |                         |                      | 0.744   |                         |                      |         |
| 6                                        | 60 (18.0)               | 30 (8.9)             |         | 41 (21.0)               | 28 (14.3)            | 0.642   |
| 7                                        | 47 (14.1)               | 53 (15.7)            |         | 38 (19.4)               | 39 (20.0)            |         |
| 8-10                                     | 77 (23.1)               | 81 (24.0)            | 0.340   | 33 (16.9)               | 36 (18.4)            | 0.678   |
| Clinical T stage, n (%)                  |                         |                      |         |                         |                      |         |
| T1                                       | 51 (15.3)               | 32 (9.5)             |         | 25 (12.8)               | 20 (10.2)            | 0.207   |
| T2                                       | 91 (27.3)               | 94 (27.9)            |         | 57 (29.2)               | 58 (29.7)            |         |
| T3 – T4                                  | 42 (12.6)               | 38 (11.3)            | 0.371   | 30 (15.3)               | 25 (12.8)            | 0.240   |
| Lymph node metastases, n (%)             | 19 (5.7)                | 25 (7.4)             |         | 10 (5.1)                | 15 (7.6)             | 0.207   |
| Distant metastases, n (%)                | 21 (6.3)                | 20 (5.9)             | 0.841   | 5 (2.5)                 | 6 (3.0)              | 0.657   |
| csPCa, n (%)                             | 124 (37.2)              | 134 (39.8)           | 0.502   | 76 (38.9)               | 84 (43.0)            | 0.163   |

PSA, prostate-specific antigen; PV, prostate volume; TRUS, transrectal ultrasonic; MRI, magnetic resonance image; PCa, prostate cancer; csPCa, clinically significant prostate cancer.

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**Table 4**  
The association between systemic and targeted biopsy in MRI-fusion biopsy ($n = 337$)

| MRI (n = 337) | Suspicious cancer lesion (−) (n = 180) | Suspicious cancer lesion (+) (n = 157) |
|---------------|--------------------------------------|---------------------------------------|
| Total PCa, n (%) | 87 (48.3) | 77 (49.0) |
| csPCa, n (%) | 63 (35) | 71 (45.2) |
| PSA category | | | |
| PSA <4 ng/mL (n = 54) | | | |
| Total PCa, n (%) | 9/29 (31.0) | 6/25 (24.0) |
| csPCa, n (%) | 2/29 (6.9) | 4/25 (16.0) |
| PSA 4–10 ng/mL (n = 196) | | | |
| Total PCa, n (%) | 44/112 (39.3) | 39/84 (46.4) |
| csPCa, n (%) | 28/112 (25.0) | 35/84 (41.7) |
| PSA >10 ng/mL (n = 87) | | | |
| Total PCa, n (%) | 34/39 (87.2) | 32/48 (66.7) |
| csPCa, n (%) | 33/39 (84.6) | 32/48 (66.7) |

P-value: 0.565, 0.399, 0.317, 0.013, 0.042, 0.055

PSA, prostate specific antigen; TRUS, transrectal ultrasound; MRI, magnetic resonance image; PCa, prostate cancer; csPCa, clinically significant prostate cancer.
For males with PSA <4 ng/mL, there was no significant difference between the method of biopsy for csPCA. For this PSA level, the detection rate of csPCA was only 11.8% (15/108), and therefore, MRI/US-fusion biopsy did not affect the results. For males with PSA >10 ng/mL, the detection rate of PCa and csPCA in the standard biopsy group was higher compared to the TBx; SBx was sufficient for diagnosing of PCa in patients with PSA >10 ng/mL. For this PSA level, the detection rate of csPCA was 78.4% (135/172), and therefore, MRI-fusion biopsy did not affect the results. Thereby, we suggest that TRUS-guided systemic random biopsy is sufficient for males with PSA <4 ng/mL or >10 ng/mL.

There are several limitations to our study. First, this is a retrospective, single-center study that may lead to a selection bias. Adjustment for possible confounding factors was made by propensity score matching, although it is possible that unknown confounding factors may persist. Further multicenter large cohort studies are required to confirm our findings. Second, the actual detection rates of csPCA may have been underestimated compared to studies using whole-gland prostatectomy or template mapping biopsy. Third, data were interpreted using PI-RADS v2 on MRI by an experienced radiologist; it is also possible that one person interpreted the MRI findings, and there was bias in that interpretation.

5. Conclusion

In conclusion, we report that the MRI/US-fusion biopsy has a high accuracy for detecting csPCA compared to standard TRUSbx in patients with biopsy-naïve men with PSA levels in the gray zone of 4–10 ng/mL. This technique, considering the good performance and cost-effectiveness of the bpMRI, is a good option for initial prostate biopsy in a clinical setting.

Author’s Contribution

Hye Jin Byun: Project development, Data Collection, Manuscript writing. Teak Jun Shin: Project development, Data analysis. Wonho Jung: Data collection. Ji Yong Ha: Data collection. Byung Hoon Kim: Project development, Manuscript editing. Young Hwan Kim: Project development.

Conflicts of interest

There is no conflict of interest.

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