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Prostate cancer detection rate in patients with fluctuating prostate-specific antigen levels on the repeat prostate biopsy

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Purpose: To evaluate whether the risk of prostate cancer was different according to the pattern of fluctuation in prostate-specific antigen (PSA) levels in patients undergoing repeat transrectal ultrasound-guided prostate biopsy (TRUS-Bx).

Methods: From March 2003 to December 2012, 492 patients underwent repeat TRUS-Bx. The patients were stratified into 3 groups based on the PSA fluctuation pattern: group 1 (continuous elevation of PSA, n=169), group 2 (PSA fluctuation with PSA velocity [PSAV] ≥ 1.0 ng/mL/yr, n=123), and group 3 (PSA fluctuation with PSAV < 1.0 ng/mL/yr, n=200).

Results: Prostate cancer was detected in 112 of 492 patients (22.8%) in the repeat biopsy set. According to the PSA fluctuation pattern, prostate cancer detection rates at repeat TRUS-Bx were 29.6% (50/169) for patients with continuously increasing PSA, 30.1% (37/123) for PSA fluctuation with PSAV ≥ 1.0 ng/mL/yr, and 12.5% (25/200) for PSA fluctuation with PSAV < 1.0 ng/mL/yr. Multivariate analysis showed that PSA fluctuation pattern and high grade prostatic intraepithelial neoplasia at initial TRUS-Bx were the predictive parameters for positive repeat biopsies. Among the 96 patients (85.7%) who underwent radical prostatectomy, no significant differences in pathologic outcomes were found according to the PSA fluctuation pattern.

Conclusions: The current study shows that the risk of prostate cancer at repeat TRUS-Bx was higher in men with a fluctuating PSA level and PSAV ≥ 1.0 ng/mL/yr than in those with a fluctuating PSA level and PSAV < 1.0 ng/mL/yr.

Keywords: Prostate-specific antigen, Prostatic neoplasms, Biopsy, Needles

INTRODUCTION

Transrectal ultrasound-guided prostate biopsy (TRUS-Bx) is the most effective method for diagnosis of prostate cancer; however, TRUS-Bx may underestimate the presence of cancer. Therefore, repeat biopsy must be considered in patients with persistent diagnostic doubts after an initial negative biopsy. In the Medicare population, the risk of repeat biopsy in men with a negative first biopsy was 11.6% at 1 year and 38.0% at 5 years [1]. Although TRUS-Bx is generally considered safe, many urologists have experienced a conflict between the risk of prostate cancer and biopsy-related morbidity that includes rectal bleeding and infectious complications [2-5]. Because of the aforementioned concerns, the use of alternative biomarkers or predicting factors has become mandatory in predicting the presence of prostate cancer in cases where clinically suspected cancer is not supported by initial histologic findings.

Prostate-specific antigen (PSA) is the universally accepted tumor marker for diagnosis of prostate cancer. Many urologists frequently encounter patients with fluctuating PSA levels

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after initial TRUS-Bx. Traditionally, these patients were considered as having a lower risk of prostate cancer than patients with steadily increasing PSA levels; however, there is paucity of firm evidence for this hypothesis [6,7].

The aim of the current study was to evaluate whether the risk of prostate cancer was different according to the PSA fluctuation pattern in patients undergoing repeat TRUS-Bx for suspected prostate cancer.

MATERIALS AND METHODS

From March 2003 to December 2012, 5,828 consecutive men with a mean age of 64.8 (±9.3) years underwent TRUS-Bx with a mean of 12.6 (±1.3) biopsy cores. The indication for initial TRUS-Bx was either an elevated PSA level (≥3 ng/mL) or abnormal digital rectal examination (DRE). Prostate cancer was detected in 2,047 men (35.1%) at initial TRUS-Bx. Of the 3,781 patients whose biopsy result was negative, 492 underwent repeat TRUS-Bx because of the high risk of prostate cancer with prior high-grade prostatic intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation of prostate, persistently elevated PSA, or increase in PSA level during follow-up. In all patients, the prostate was routinely biopsied bilaterally near the base, midgland, and apex with at least six biopsies per side. All biopsy cores were reviewed by a single board-certified uropathologist (K.Y.C.) using contemporary diagnostic criteria. In the presence of prostate cancer, either radical prostatectomy or radiation therapy was recommended.

After approval by the Institutional Review Board at Seoul National University Bundang Hospital (B-1310-222-109), clinical and pathologic data, including patient age, PSA, PSA density, PSA velocity (PSAV), and PSA fluctuation pattern were analyzed using our computerized database. PSAV was calculated as PSA level at the time of second biopsy minus PSA level at the time of first biopsy divided by the time elapsed in years between two measurements. PSA fluctuation was defined as a PSA series with at least one PSA value lower than the one immediately preceding it. The patients were stratified into three groups based on the PSA fluctuation pattern: group 1 (continuous elevation of PSA, n=169), group 2 (PSA fluctuation with PSAV≥1.0 ng/mL/yr, n=123), and group 3 (PSA fluctuation with PSAV<1.0 ng/mL/yr, n=200).

All statistical analysis was performed using IBM SPSS ver. 19.0 (IBM Co., Armonk, NY, USA). Demographics and clinical parameters were analyzed with the chi-square test for categorical variables and the one-way analysis of variance test or the Kruskal-Wallis test, as appropriate for continuous variables. Two-sided null hypotheses of no difference were rejected if *P*-values were less than 0.05.

Table 1. Baseline patient characteristics

Characteristic	Value
Age (yr)	65.2±7.8
Body mass index (kg/m^2)	23.7±4.8
PSA at initial biopsy (ng/mL)	8.2±0.3
PSA at repeated biopsy (ng/mL)	9.9±0.4
Prostate volume (mL)	48.8±21.1
Transition zone volume (mL)	25.7±17.6
PSA density (ng/mL/mL)	0.16±0.09
PSA velocity (ng/mL/yr)	1.05±1.90
Abnormal DRE	48 (9.8)
Abnormal TRUS	73 (14.8)
Months interbiopsy interval	16.0±12.1

Values are presented as mean±standard deviation or number (%).
PSA, prostate-specific antigen; DRE, digital rectal examination; TRUS, transrectal ultrasound.

RESULTS

The baseline characteristics of the cohort are presented in Table 1. The mean age of the patients was 65.2 years; their mean PSA levels before the initial and repeat biopsy sets were 8.2 and 9.9 ng/mL, respectively (P=0.016). Only 11 of the 492 patients (2.2%) experienced adverse events after repeat TRUS-Bx, with acute prostatitis in 7 patients, rectal bleeding in 3 patients, and acute urinary retention in 1 patient.

Prostate cancer was detected in 112 of 492 patients (22.8%) in the repeat biopsy set; 6 of 40 patients (15.0%) in the third biopsy set; and 1 of 4 patients (25.0%) in the fourth biopsy set. According to the PSA fluctuation pattern, prostate cancer detection rates at repeat TRUS-Bx were 29.6% (50/169) for patients with continuously increasing PSA, 30.1% (37/123) for PSA fluctuation with PSAV≥1.0 ng/mL/yr, and 12.5% (25/200) for PSA fluctuation with PSAV<1.0 ng/mL/yr.

There was no statistical significance between patients with and without prostate cancer at repeat TRUS-Bx for age (66.8 years vs. 64.7 years, P=0.089), body mass index (23.6 kg/m^2 vs. 23.7 kg/m^2, P=0.867), and prostate volume (46.3 mL vs. 49.4 mL, P=0.249). Patients with prostate cancer had higher PSA levels at repeat TRUS-Bx (10.2 ng/mL vs. 9.1 ng/mL, P=0.012), higher PSA density (0.21 ng/mL/mL vs. 0.14 ng/mL/mL, P=0.041), and higher PSAV (1.23 ng/mL/yr vs. 0.91 ng/mL/yr, P<0.001). Multivariate analysis showed that PSA fluctuation pattern and HGPIN at initial TRUS-Bx were the predictive parameters for positive biopsies (Table 2).

Ninety-six patients (85.7%) underwent radical prostatectomy. Table 3 presents the pathologic results of the surgical specimen. Pathologic stage was organ confined in 90.6% of