ORIGINAL ARTICLE

Application of transrectal ultrasound-guided repeat needle biopsy in the diagnosis of prostate cancer in Chinese population: A retrospective study

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Background: Transrectal ultrasound-guided repeat needle biopsy (TUGRNB) is widely used for diagnosis of prostate cancer (PCa). However, significance of TUGRNB in Chinese population was rarely reported. A retrospective study was conducted to evaluate the significance of TUGRNB applied in prediction of PCa in Chinese population. **Materials and Methods:** A total of 960 from January 2009 to December 2012 were included. Repeat needle biopsy rate and PCa positive detection rate were evaluated. Relationship between prostate specific antigen (PSA) levels and PCa positive rates was analyzed. **Results:** PCa positive detection rate after initial needle biopsy was 28.4%, which was lower than the rate of repeat needle biopsy (40%). The rate for immediate transurethral resection (TUR), surgery after initial needle biopsy, was 27.1%, however with a low PCa positive detection rate (0.66%). The repeat needle biopsy rate was lower compared with the initial biopsy rate ($P < 0.05$). Meanwhile, immediate TUR rate was significantly higher than that of the repeat needle biopsy rate ($P < 0.05$). Among the three groups, the PCa positive detection rate in repeat needle biopsy group was the highest. In subgroups with different PSA levels, the PCa positive rate increased with the elevation of PSA level. In cases with PSA > 20 ng/ml, PCa positive rate was significantly higher than those with PSA < 20 ng/ml ($P < 0.05$). **Conclusion:** PCa positive detection rate following repeat needle biopsy in Chinese population was higher, although the repeated needle biopsy rate was still in a low level. TUGRNB should attract more attention in the diagnosis of PCa.

Key words: Prostate cancer, prostate specific antigen, repeat needle biopsy

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INTRODUCTION

Prostate cancer (PCa) has become one of the most common types of cancer in urinary system and the increased incidence and mortality seriously affect health in the elder male population. In China, the incidence of PCa climbed to 10 in 0.1 million persons.[1] Therefore, early detection of PCa is urgently necessary for the disease treatment.

Prostate-specific antigen (PSA) is present in the serum of men with healthy prostates but is often elevated in the presence of PCa or other prostate disorders. However, PSA is still a controversial indicator for PCa, because it may also indicate prostatitis or benign prostatic hyperplasia (BPH).[2,3] Besides PSA, other risk factors also contribute to development of PCa, including age, a positive family history, abnormal digital rectal examination (DRE) and ethnicity.[4,5]

Prostate needle biopsy technique was firstly established in 1905. Until 1989, Hodge *et al*. proposed six-needle biopsy technique following transrectal ultrasonography.[6] Recently, prostate needle biopsy has become a systematic

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and standard procedure for diagnosis of PCa. With the development of needle biopsy technique, accurate diagnosis was improved, and the PCa positive detection rate increased to about 20–40%.[7] However, an initial needle biopsy was still accompanied with a high negative detection rate. Therefore, repeat needle biopsy is essential for the diagnosis of PCa in some cases.[8] Nevertheless, application and significance of repeat needle biopsy were rarely reported in Chinese patients.[9] To track the utility of repeated needle biopsy in diagnosis of PCa in China, a retrospective analysis was carried out.

MATERIALS AND METHODS

Study design and participants

From January 2009 to December 2012, 960 patients who underwent prostate biopsy were collected in the First Affiliated Hospital of Soochow University, the Second Affiliated Hospital of Soochow University and Suzhou Kowoon Hospital (Shanghai Jiaotong University). This study was under the approval of ethics of Suzhou Kowloon Hospital Affiliated to Shanghai Jiaotong University.

All biopsies were performed according to the standard guideline.[10] At least one of abnormalities of the three factors (PSA, DRE, and transurethral resections [TURs]) was included as the criteria for biopsy. After exclusion of unqualified cases, the cases were divided into three groups: Group 1 (initial needle biopsy, 779 cases), Group 2 (repeat needle biopsy, thirty cases), and Group 3 (TURs after the initial negative biopsy, 151 patients). Inclusion criteria for initial needle biopsy were: (1) Abnormality of DRE with any PSA value; (2) abnormality of ultrasonography or magnetic resonance imaging with any PSA value; (3) PSA value >10 ng/m with any free/total PSA (f/t PSA) and PSA density (PSAD); (4) PSA value between 4 and 10 ng/ml with abnormal f/t PSA or PSAD. Inclusion criteria for repeat needle biopsy: Atypical small acinar proliferation (ASAP) and prostatic intraepithelial neoplasia (PIN) were observed after initial biopsy; (2) PSA >10 ng/ml with any f/t PSA and PSAD value; (3) PSA 4–10 ng/ml with any abnormality in f/t PSA, PSAD, DRE, or TURs; (4) PSA 4–10 ng/ml with normal f/t PSA, PSAD, DRE or TURs, but PSA >10 ng/ml was observed at least 2 times or prostate-specific antigen velocity was higher than 0.75 ml/year during the follow-up.[11]

Procedures and variables assessment

The positive rate of PCa among the three groups was analyzed by pathological method, and the rate of the repeat prostate biopsy of Group 2 and the rate of immediately TURs after the initial negative biopsy of the Group 3 were also evaluated. The cases in Group 1 were divided into five subgroups according to the PSA levels and into five subgroups according to different pathological results, including PCa, BPH with ASAP, BPH with PIN, BPH with chronic prostatitis (CP) and single BPH. Then, positive rates and the PSA levels of the subgroups were evaluated. Serum PSA level was measured using enzyme-linked immunosorbent assay method based on the instruction of assaying kit (CanAg, Sweden).

Statistical analysis

The quantitative data were presented with mean and standard deviation, and qualitative data were presented with the real values. All the data were analyzed by SPSS 16.0 software (IBM, LA, USA). ANOVA was used to analyze the difference among groups. Least significant difference and *post hoc* Tukey's test followed ANOVA were used to analyze the difference between inter-groups. Chi-square test was used to analyze the difference of the qualitative data. $P < 0.05$ was considered as significant difference. Area under curve (AUC) of PSA levels with PCa positive rate in Group 1 was also analyzed.

RESULTS

A total of 779 patients (age from 45 to 91 years, average: 69.4 years) were included in Group 1. There were thirty patients (age from 54 to 90 years, average: 67 years) in Group 2. In Group 3, 151 patients (age from 53 to 87 years, average: 69.6 years) were included.

In initial needle biopsy group, PCa positive rate was 28.4% (221/779). By contrast, in repeat needle biopsy group, the PCa positive detection rate was 40% (12/30), and the repeat biopsy rate was 5.38% (30/558). In Group 3, the PCa positive rate was 0.66% (1/151), and the rate of immediate TURs after initial negative biopsy was 27.1% (151/558) [Table 1].

The repeat biopsy rate was lower compared with the initial biopsy one ($P < 0.05$). Meanwhile, the immediate TURs rate was significantly higher than that of the repeated biopsy rate ($P < 0.05$). Among the three groups, positive rate of the Group 2 was the highest and Group 3 was the lowest.

In subgroups of Group 1 with different PSA levels, the PCa positive detection rate increased with the elevation of PSA. In cases with PSA >20 ng/ml, PCa positive rate was significantly higher than those with PSA <20 ng/ml ($P < 0.05$) [Table 2]. The PSA values in different subgroups with different pathological diagnosis were shown in Figure 1 and Table 3. The PSA values in the five groups underwent ANOVA; significant difference was found when PCa positive group was compared with non-PCa positive groups ($P < 0.05$).

AUC for PCa positive rate with PSA levels was shown in Figure 2. The value of AUC was 0.767 (confidence interval: 0.9; sensitivity and specificity: 0.462), and the best diagnosis inflection point of PSA was 22.785 ng/ml

Table 1: The comparison of prostate cancer positive rate in different groups

	Group 1	Group 2	Group 3
Positive	221	12	1
Negative	558	18	150
Total	779	30	151
PCa positive rate (%)	28.4**	40**	0.66

Group 1, Group 2 and Group 3 represented initial needle biopsy, repeat needle biopsy and TURs after the initial negative biopsy, respectively. **P<0.01 compared with Group 3. PCa=Prostate cancer

Table 2: The distributions of prostate cancer positive rate in different prostate specific antigen values

	Subgroups					Total
	A	B	C	D	E	
	PSA values (ng/ml)					
	≤4	4.1-10	10.1-20	20.1-50	>50	
PCa						
Positive						
Cases	5	33	33	62	88	221
Percentage	9.4	15.8	14.3	33.7*	86.3**	28.4
Negative						
Cases	48	176	198	122	14	558
Percentage	90.6	84.2	85.7	66.3	13.7	71.6
Total						
Cases	53	209	231	184	102	779

*In Group D indicated P<0.05 compared with A, B and C, **In Group E indicated P<0.01 compared with A, B, C and D. PSA=Prostate specific antigen; PCa=Prostate cancer

Table 3: The distribution of prostate specific antigen levels in different pathological conditions

Groups	Cases	Percentage	PSA values (ng/ml)
PCa	221	28.4	54.48±63.81*
BPH with ASAP	56	7.2	17.08±18.85
BPH with PIN	32	4.1	18.18±20.34
BPH with CP	127	16.3	17.73±15.30
BPH	343	44.0	15.18±14.19
Total	779	100	27.00±40.25

*P<0.05 in PCA group compared with other four groups. PCa: Prostate cancer; PSA=Prostate specific antigen; BPH=Benign prostatic hyperplasia; ASAP=Atypical small acinar proliferation; PIN=Prostatic intraepithelial neoplasia; CP=Chronic prostatitis

DISCUSSION

In this study, 960 cases were finally included and divided into three groups. All of the cases underwent needle biopsy and PCa positive detection rate was 28.4%, while thirty cases underwent repeat needle biopsy, with a positive rate of 40%. Obviously, compared with other studies, repeat needle biopsy rate was lower, whereas positive detection rate was higher.[12,13]

Campos-Fernandes *et al*. reported that PCa positive detection rates after the second, third and fourth repeat needle biopsy were 18%, 17%, and 14%, respectively.[12] Naya *et al*. reported that the PCa positive detection rate after initial needle biopsy was 33.8%. The repeat needle biopsy rate was 16.1% with the PCa detection rate of 18.3%.[13] Importantly, high-grade PIN value was not an ideal indication for repeat needle biopsy. Djavan *et al*. reported that 1051 cases with PSA of 4–10 ng/ml underwent four repeats of needle biopsy and PCa rates were 22%, 10%, 5%, and 4%, respectively. They also suggested that 1–2 repeat needle biopsy was appropriate, and three or more time repeat needle biopsy was not necessary.[14] Ploussard *et al*. reported that PCa positive rate after repeat needle biopsy was 7.0% and the initial needle biopsy was accurate to predict PCa. PSA, PSAD, volume and f/t PSA were helpful for the prediction.[15] In addition, Barbera *et al*. found that the PCa positive rate after repeat needle biopsy was 27.1%. Moreover, they found that the PCa antigen 3 (PCA 3) value in PCa positive cases were sixty, while decreased to 34 in PCa negative cases. Accordingly, initial biopsy PCA 3 based nomogram is reconstructed to indicate high predictive accuracy, especially for high-grade PCa and improves the ability to predict biopsy outcomes.[16,17] Based on above reports, PCa positive rate after repeat needle biopsy was at the range of 16.7–27.1%, which was much lower than that found in our study (40%). In addition, the repeat needle biopsy rate in our study was much lower (5.38%) than those in previous

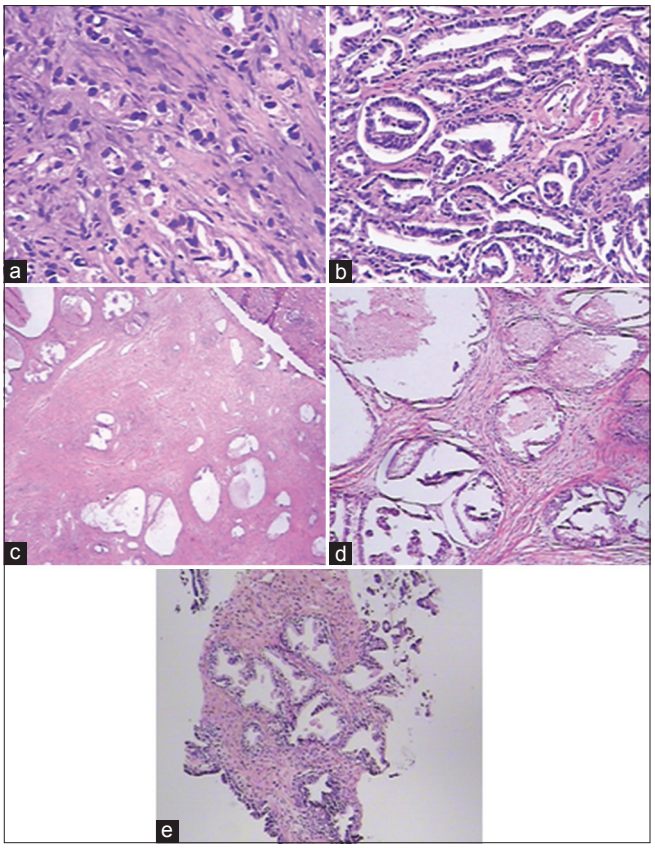

Figure 1: Pathological characteristics of prostate cancer, (a) prostate cancer; (b) benign prostatic hyperplasia with atypical small acinar proliferation; (c) benign prostatic hyperplasia with prostatic intraepithelial neoplasia; (d) benign prostatic hyperplasia with chronic prostatitis; (e) benign prostatic hyperplasia

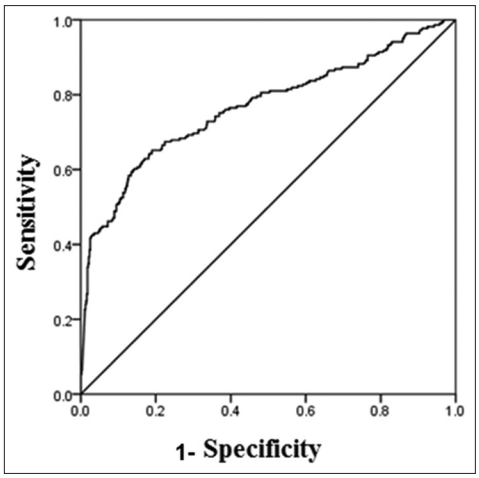

Figure 2: Area under curve for prostate cancer positive rate with prostate-specific antigen levels

publications (16.1–31%). In Chinese population, one related study also applied transrectal ultrasound-guided repeat prostate biopsy to predict PCa.[9] However, Li *et al*. mainly focused on the analysis of the multi-variables possibly determining the positive rate, however, did not compare the positive rate after initial needle biopsy, repeat needle biopsy, and TURs after the initial negative biopsy. In addition, they reported a positive rate of PCa prediction about 31.8%, which was much lower than that in our study.

In this study, 779 cases underwent initial needle biopsy, and 558 cases were found to be PCa negative. A total of 151 cases immediately experienced TUR surgery, and the rate was 27.1%. Finally, only one case was found to be PCa positive (0.66%). Compared the PCa positive detection rate in the three groups, we found that Group 3 (immediate TUR) had the lowest PCa positive rate, and Group 2 (repeated needle biopsy) displayed the highest PCa positive rate. The PCa positive rate in Group 3 was the lowest, indicating that immediate TURs following initial negative needle biopsy is not an ideal approach to diagnose PCa.[18] The possible reason for this discrepancy could be due to the complex structure of prostate. Structurally, prostate consists of transitional zone (70%, volume), central zone (25%, volume), and peripheral zone (5%, volume). Normally, 64% of the PCa was found in peripheral zone, 8% in central zone, and 24% in transitional zone. In fact, during TUR surgery, most of the tissues were from central zone and transitional zone. The tested tissues were rarely from peripheral zone, leading to a low PCa positive detection rate. Therefore, immediate TUR surgery was not an effective prediction for PCa. With PSA <20 ng/ml and pathological characteristic of single BPH or BPH and CP in combination, the PCa negative cases after initial needle biopsy could be treated by 5ARIs.[19,20] In the 3–6-month follow-up, PSA should be measured again to make sure whether repeat needle biopsy was required.

PSA is present in the serum of men with healthy prostates but is often elevated in the presence of PCa or other prostate disorders while BPH, CP, ASAP, and PIN could also lead to elevation of PSA. Based upon "Reduction by Dutasteride of PCa Event," the level of PSA could be an important indicator for PCa diagnosis.[21] Interestingly, 5-alpha reductase inhibitors (5-ARIs) could inhibit the advance of PCa[19,20] and also benign PCa. Therefore, treatment with 5-ARIs was a beneficial approach to avoid unnecessary repeated needle biopsy.

CONCLUSION

Although PCa positive detection rate following repeat needle biopsy in our study was higher, the repeat needle biopsy rate in Chinese population was still in a low level. Possible reasons might include racial differences, attitudes toward needle biopsy technique. Hence, we need to pay more attention to or strengthen the significance of repeat needle biopsy for the prediction of PCa.

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Conflicts of interest

There are no conflicts of interest.

AUTHORS' CONTRIBUTION

YW, XW, JU, JO contributed in designing, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. WS, YZ, JH, DW, JP, YS, and BX collected the data and analyzed the data.

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