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The sufficiency of 6 core sextant prostate biopsy in patients with prostate specific antigen (PSA) values over 20 ng/mL

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Summary
Objective: In this study, we aimed to investigate sufficiency of 6 core prostate biopsy in patients with PSA levels elevated above 20 ng/mL.
Materials and methods: The medical record of the patients who received prostate biopsy at our institution between August 2011 to August 2016 who had serum total PSA values above 20 ng/mL, were reviewed retrospectively. In this study, we included 40 patients who received 6 core prostate biopsy and 40 patients who received 12 core prostate biopsy. A total number of 80 patients were enrolled in this study. Patients were divided into two groups, a 6 core biopsy group and a 12 core biopsy group. These groups are compared according to age, total PSA, prostate volume and final pathological diagnosis.
Results: Based on final pathological diagnosis, 2 patients (5%) had benign pathology and 38 patients (95%) had PCa in both group 1 and 2. The cancer detection rate in both groups was 95%. Although there were higher values of mean age, mean total PSA, and mean prostate volume in group 1, there was no statistically significantly difference at this variables in both groups.
Conclusion: Although taking 6 core biopsies is not recently recommended, we proved that 6 core biopsy is adequate for patients with PSA values above 20 ng/mL.

KEY WORDS: Prostate cancer; Biopsy; Detection rate; Core number.

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INTRODUCTION

Prostate cancer (PCa) is the most common cancer in men worldwide (1). The diagnosis of PCa depends on sufficient tissue sampling of the prostate gland with prostate biopsy (2). The technique of prostate biopsy has evolved through the years with the advent of new technologies. In 1989 *Hodge et al.* first described *transrectal ultrasound* (TRUS) guided sextant biopsy method (3). Since then, this method has become the worldwide most popular and PCa detection has significantly improved. Its limitations were soon discovered. Many investigator reported false-negative rates of up to 20-25% for the sextant biopsy (4). This naturally resulted in the development of refinements to the TRUS-guided sextant biopsy. *Stamey et al.* suggested directing the biopsy more laterally (5). Multiple biopsy schemes were subsequently proposed to enhance cancer detection by increasing the number and revising the

location of cores (6). Six core sextant biopsy is no longer considered adequate. Recently, 10 to 12 core biopsies are recommended and biopsies with > 12 cores are not being significantly more conclusive (7). Patients with prostate spesific antigen (PSA) levels > 20 ng/mL are classified as high risk group for diagnosis of PCa (8). This risk increases with age and these patients have higher possibility to have locally advanced or metastatic disease at the time of diagnosis. In the present study, we aimed to investigate sufficiency of 6 core sextant prostate biopsy in patients with PSA levels elevated above 20 ng/mL. We hypothesized that there is no significant difference in cancer detection rate between 6 core and 12 core prostate biopsies of men presenting PSA values of above 20 ng/mL.

MATERIALS AND METHODS

The medical record of the patients who received prostate biopsy at our institution between August 2011 to August 2016 and had serum total PSA values above 20 ng/mL, were reviewed retrospectively. In the present study, we included 40 patients who received 6 core prostate biopsy and 40 patients who received 12 core prostate biopsy. We excluded the patients who have chronic diseases (diabetes, hyperlipidemia, hypertension, cardiovascular disease), malignancy, psychiatric disorders, acute infections, a history of urinary tract surgery, a prior diagnosis of PCa and a history of irradiation. We also excluded patients with PSA < 20 ng/mL. After obtaining informed consent from patients, all biopsies were taken transrectally with ultrasonography guidance using a 25 cm 18 gauge, side-notch cutting (Tru-cut) needle.
The biopsy was applied with patient in lateral decubitus position with periprostatic nerve blockage. A total number of 80 patients were enrolled in this study. The clinic-biological features of patients were recorded. Patients were divided into two groups, a 6 core biopsy group (Group 1) and a 12 core biopsy group (Group 2). These groups were compared according to age, total PSA, prostate volume and final pathological diagnosis. We also identified the cancer detection rate and Gleason scores of these groups.

Statistical analysis
The conformity of variables to normal distribution was assessed with the Shapiro Wilk test. Descriptive statistics

for variables with a normal distribution and categorical variables were shown as mean ± *standard deviation* (SD) and percentage (%), respectively. Student's t-test and chi-square test were used for inter group analyses of continuous variables. More than two independent average compared with ANOVA test and Kruskal Wallis test.

The data analysis was performed using Statistical Package for the Social Science (*SPSS Inc, Chicago, Illinois, USA*) version 22.0 and a p value of < 0.05 was considered as significant.

RESULTS

A total of 80 patients participated in this study. The mean age of all patients was 72.2±8.4, the mean total PSA was 126.0 ± 101.3 ng/mL, the mean prostate volume was 50.4 ± 41.6 mL and overall cancer detection rate was 95.0%. Clinical and demographic characteristics of all study patients are listed in Table 1. Based on final pathological diagnosis, 2 patients (5%) had benign pathology and 38 patients (95%) had PCa in both group 1 and 2. The cancer detection rate in both groups was 95%.

The Gleason score was found to be 6 in 3 (7.9%), 7 in 14 (36.8%) and ≥ 8 in 21 (55.3%) patients who were diagnosed as PCa in group 1 and from the other side 6 in 4 (10.5%), 7 in 11 (28.9%) and ≥ 8 in 23 (60.5%) patients who were diagnosed as PCa in group 2. The differances in Gleason scores was not determined to be statistically significant (p= 0.783). Although there was higher values of mean age, mean total PSA, and mean prostate volume in group 1, there was no statistically significantly difference at this variables in group 1 and 2 (Table 2).

The cancer detection rates of both groups were similar (p = > 0.999).

DISCUSSION

PCa is still a major health problem among males all over the world. Despite efforts made to identify new serum and biologic markers of disease and refinement of imaging modalities, TRUS guided biopsy is still most important diagnostic tool. Important improvements in the prostate biopsy have evolved though the past century. Modern technique of prostate biopsy first began with the

Table 1.
Clinical and biological characteristics of all patients (n = 80).

	Mean (SD)
Age (years)	72.2 (± 8.4)
PSA (ng/ml)	126.0 (± 101.3)
Prostate volume (ml)	50.4 (± 41.6)
Pathology (n, %)	
BPH	4 (5.0)
PCa	76 (95.0)
Gleason score (n, %)	
6	7 (9.2)
7	25 (32.9)
≥ 8	44 (57.9)

PSA: prostate-specific antigen, BPH: benign prostatic hyperplasia; PCa: prostate cancer; SD: standard deviation.

Table 2.
Comparison of clinical characteristics of 2 groups.

	Group 1	Group 2	P value
Age (years)	74.1 ± 6.8	70.3 ± 8.9	0.072
PSA (ng/ml)	139.4 ± 123.0	112.6 ± 72.7	0.265
Prostate volume (ml)	54.4 ± 52.5	46.4 ± 26.9	0.358
Pathology (n, %)			
BPH	2 (5.0)	2 (5.0)	> 0.999
PCa	38 (95.0)	38 (95.0)	> 0.999
Gleason score (n, %)			
6	3 (7.9)	4 (10.5)	0.689
7	14 (36.8)	11 (28.9)	0.602
≥ 8	21 (55.3)	23 (60.5)	0.783

PSA: prostate-specific antigen, BPH: benign prostatic hyperplasia; PCa: prostate cancer.

study of *Hodge et al*. Their method involved taking biopsies from apex, middle and base of each prostate gland para-sagitally. In addition to these six anatomic sites they suggested to take biopsy from hypoechoic regions (3). Since then, this method has become the worldwide most popular and PCa detection has significantly improved. In 1995, *Stamey et al*. modified the sextant method and directed the biopsy more laterally to peripheral zone where most PCa are located. They achieved 20-25% more cancer detection rate than Hodges method (5). Then many researchers investigated the acceptable number of core biopsies for diagnosis. They make an effort to improve the negative predictive value of prostate biopsy. *Guichard et al*. found the cancer detection rates of 6, 12, 18 and 21 core prostate biopsies were 31.7%, 38.7%, 41.5% and 42.5% respectively (9). Similarly to this study, *Ceylan et al*. reported cancer detection rates of 8, 10, 12, 16, and 20 core prostate biopsies as 18.3%, 14.8%, 24%, 22.1%, and 30.3% respectively (10).

The logic of these studies is based on increasing the possibility of detecting PCa by increasing the sample. Six core biopsy is no longer considered adequate. In present study, we found there is no significant difference in cancer detection rate between 6 core and 12 core prostate biopsies of men presenting PSA values of above 20 ng/mL. According to current literature, 6 cores biopsy is not recommended but may be sufficient especially in patients with high PSA (over 20 ng/mL).

Prostate cancer risk was summarized using the D'Amico classification and PSA level is one of three variables on which the risk classification is based (11). According to D'Amico scheme, patients with a PSA over 20 ng/mL are classified as high risk and these patients have higher possibility to have locally advanced or metastatic disease at the time of diagnosis. *Stephenson et al*. reported that the 15 years prostate cancer specific mortality was 22% in patients with PSA of 20.1-50 ng/mL and 4-11% in those with PSA < 20 ng/mL and suggested that a PSA > 20 ng/mL may indeed be considered a high-risk factor (12). *Heyns et al*. reported that a PSA level > 50 ng/mL was associated with a 96% positive predictive value for prostate cancer (13). *Gerstenbluth et al*. reviewed the records of 1,250 patients undergoing TRUS guided prostate biopsy and identified 187 men (15%) presenting with PSA greater than 20 ng/mL. Of these 187 men, 157

(84.0%) were diagnosed with prostate cancer on initial biopsy and 12 patients had repeat biopsy and 6 of these eventually diagnosed PCa. Overall, 163 of the 187 men (87.2%) were diagnosed with prostate cancer by biopsy. They suggested that carefully selected elderly patients with severe comorbidities may not require biopsy before androgen ablative therapy since PSA is highly accurate in diagnosing prostate cancer at levels greater than 50 ng/mL (14). *Anai et al.* recommended that highly select symptomatic men with extremely high serum PSA could be started on immediate androgen ablative therapy even without a tissue diagnosis of prostate cancer (15). In the present study, we found 95% cancer detection rate and detected that 90.8% of all patients had high risk PCa according to their final pathological diagnosis.

The morbidity of prostate biopsy is minimal, reported at < 1% (4). Early complications of prostate biopsies include hematospermia (37%), hematuria more than 1 day (14.5%), rectal bleeding more than 2 days (2.2%) and urinary retention that required observation or intervention (1.8%). Delayed complications of prostate biopsies are urinary tract obstruction (10.9%), fever (2.9%), sepsis (0.1%) (16). *Naughton et al.* reported similar complication results in a prospective evaluation of 6 and 12 core biopsies (17). Contrary to this study, *Feliciano et al.* reported that the increased number of biopsy cores contributed to increased morbidity associated with prostate biopsy (18). We thought that there is not necessary to increase the core number of prostate biopsy if it have not additional contribution to cancer detection.

Our study has limitations. First limitation of our study is its retrospective nature. Not assessing the complications of biopsies was the second limitation of our study. The other limitation of this study is small sample size and this limitation could affect the interpretation of results. A larger series of patients will provide a more accurate picture.

CONCLUSIONS

Although taking 6 core biopsies is not recently recommended, we proved that 6 core biopsy is adequate for patients with PSA values above 20 ng/mL. Our results may provide additional information for importance of 6 core biopsy and we believe that a large-scale, multicenter, prospective study will provide a more accurate picture for the clinical significance of 6 core sextant prostate biopsies of men presenting PSA values of above 20 ng/mL.

As a result, 6 core may be sufficient if prostate biopsy can not be tolerated especially in patients with high PSA.

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