Is It Effective to Perform Two More Prostate Biopsies According to Prostate-Specific Antigen Level and Prostate Volume in Detecting Prostate Cancer?

Prospective Study of 10-Core and 12-Core Prostate Biopsy

Byung Il Yoon, Tae Seung Shin, Hyuk Jin Cho, Sung-Hoo Hong, Ji Youl Lee, Tae-Kon Hwang , Sae Woong Kim

Department of Urology, The Catholic University of Korea, College of Medicine, Seoul, Korea

Corresponding Author:

Sae Woong Kim, MD
Department of Urology, The Catholic University of Korea College of Medicine, Seoul, Korea
Seoul St Mary's Hospital, 505 Banpo-dong, Seocho-gu, Seoul, 137-701, Korea

Tel: +822 2258 6226
Fax: +822 599 7839
E-mail: ksw1227@catholic.ac.kr

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Purpose: To evaluate the effectiveness of 2 more core prostate biopsy protocol in detecting the prostate cancer (PCa) by comparing 10-core prostate biopsy with 12-core according to the prostate-specific antigen (PSA) level and the prostate volume.

Materials and Methods: A total of 474 men with elevated serum levels of PSA between 2.5 and 20.0 ng/mL, regardless of abnormal finding on digital rectal examination and transrectal ultrasonography, received transrectal ultrasound-guided prostate biopsies. The patients were prospectively randomized to undergo 10-core (group 1, n = 351) or 12-core (group 2, n = 123) biopsy. The PCa detection rates were assessed and compared according to the serum level of PSA and prostate volume.

Results: Of 474 men, 128 (27.0%) were diagnosed with PCa. The PCa detection rates of 10-core and 12-core biopsies were 26.4% and 28.4%, respectively (P = .378). There was no difference in cancer detection rates according to PSA level in both groups. Comparing the cancer detection rates according to the prostate volume (< 40 mL and ≥ 40 mL), the patients with prostate volume ≥ 40 mL showed higher cancer detection rates in 12-core biopsy group (26.9%) compared with 10-core biopsy group (16.4%) (P < .05).

Conclusion: The overall cancer detection rates showed no differences in both groups. But the 12-core biopsy was a more efficient method in men with a prostate volume of ≥ 40 mL, compared to the 10-core biopsy.

Keywords: prostate, prostatic neoplasms, prostate-specific antigen, biopsy

INTRODUCTION

As serum prostate-specific antigen (PSA) test and digital rectal examination (DRE) have become generalized for the screening of the prostate cancer (PCa), the number of patients receiving the prostate biopsy is increasing. Since Hodge and colleagues proposed transrectal ultrasound (TRUS)-guided sextant prostate biopsy,[1] it has become the standard method for the diagnosis of the PCa. But sextant biopsies have false-negative rates ranging from 20% to 30% in the PCa detection.[2,3]

Because of not considering prostate volume (PV) in sextant biopsy, several studies have suggested the extended prostate biopsy to improve the cancer detection rates compared to standard sextant prostate biopsy;[4] however, this issue is still under debate. While some authors reported that extended prostate biopsy did not only improve the PCa detection rates, but also increased morbidity rates due to increased biopsy samples.

Recently, many urologists are more labile to perform extended prostate biopsy rather than the conventional sextant biopsy. Most of the studies reported previously are on the comparison of sextant with extended biopsies. Our aim was to evaluate the PCa detection rates of extended biopsy of 10-core and 12-core for the patients whose serum level of PSA elevated to 2.5 to 20.0 ng/mL regardless of TRUS or DRE findings, as well as the PV.

MATERIALS AND METHODS

The protocol of this study was first approved by a central ethical committee (Catholic Medical Center, The Catholic University of Korea College of Medicine, Seoul, Korea, No. KC11RISE0506) and then by the respective local ethical committees.

Between May 2009 and July 2010, 474 candidates for the prostate biopsy with elevated serum levels of PSA (2.5 to 20.0 ng/mL) regardless of TRUS or DRE findings were included in the study. A written informed consent was obtained from each participant.

Patients were randomized to receive 10- or 12-core biopsies; 351 patients received 10-core prostate biopsy (Group 1) and 123 subjects received 12-core prostate biopsy (Group 2). In addition to the standard sextant biopsy technique, 4 or 6 more biopsy cores were obtained from the lateral peripheral zone (Figure). In 10-core prostate biopsy, the lateral peripheral zone biopsy cores were taken from the base, midgland. In 12-core prostate biopsy, apex of the lateral peripheral zone biopsy cores was added to 10-core prostate biopsy.

All the men received prophylactic oral ciprofloxacin starting pre-biopsy and continued twice daily for 5 days. Prior to the prostate biopsy, soap-saline enema was performed for the patients, and quinolones antibiotics were injected intravenously.

After the prostate biopsy, oral ciprofloxacin was continued for additional 7 days. The patient was discharged the day after the prostate biopsy after confirming the absence of complications, such as hematuria, acute prostatitis, rectal bleeding, vasovagal syncope, and acute urinary retention.

Prostate volume was measured by the application of Prolate Ellipsoid Formula (PV = 0.5233 × transverse length × vertical length × anteroposterior length).[5] We evaluated the PCa detection rates of 10-core and 12-core biopsy group accord-

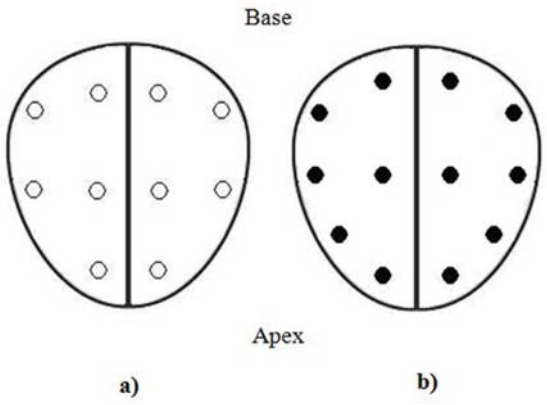

Figure. Location of biopsy taken. a) Position of 10-core biopsy; b) Position of 12-core biopsy.

Table 1. Clinical characteristics and cancer detection rate of the patients.

	Total	10-core prostate biopsy	12-core prostate biopsy	*P*
Number of patients	474	351	123	
Age, y	65.9 ± 9.7	66.5 ± 9.5	64.4 ± 10.2	.053
Prostate-specific antigen, ng/mL	10.9 ± 15.3	10.5 ± 13.3	12.1 ± 20.1	.411
Prostate volume, mL	42.4 ± 20.7	42.6 ± 22.4	42.0 ± 14.9	.723
Cancer detection rate, n (%)	128 (27.0)	93 (26.4)	35 (28.4)	.378

Table 2. Prostate cancer detection rate according to the serum level of prostate-specific antigen and prostate volume.

	Total	10-core prostate biopsy	12-core prostate biopsy	*P*
Prostate-specific antigen, ng/mL				
2.5 to 4.0	8/57 (14.0 %)	5/38 (13.1%)	3/19 (15.7%)	.540
4.1 to 10.0	66/293 (22.5 %)	50/219 (22.8%)	16/74 (21.6%)	.484
10.1 to 20.0	54/124 (43.5 %)	38/94 (40.4%)	16/30 (53.3%)	.152
Prostate volume, mL				
< 40	86/259 (33.2%)	68/199 (34.1%)	18/60 (30.0%)	.331
≥ 40	42/215 (19.5%)	25/152 (16.4%)	17/63 (26.9%)	.049

ing to the PV (< 40 mL and ≥ 40 mL).

Furthermore, we evaluated the PCa detection rates of 10-core and 12-core biopsy group according to serum levels of PSA (2.5 to 4.0 ng/mL, 4.1 to 10.0 ng/mL, and 10.1 to 20.0 ng/mL).

Data were analyzed using SPSS software (the Statistical Package for the Social Sciences, Version 12.0, SPSS Inc, Chicago, Illinois, USA). To assess the differences between the groups, independent samples *t* test and Pearson Chi-Square test were used. *P* values less than .05 were considered statistically significant.

RESULTS

The mean age of the patients was 62.9 ± 9.7 years. The mean level of PSA and mean PV were 10.9 ± 15.3 ng/mL and 42.4 ± 20.7 mL, respectively, and there were no differences between the two groups (*P* = .411 and *P* = .723).

The overall PCa detection rate was 27.0% (128/474), and the rate of 10-core and 12-core biopsies were 26.4% (93/351) and 28.4% (35/123), respectively (*P* = .378). The characteristics and overall PCa detection rate of the 474 patients undergoing 10-core and 12-core biopsies are shown in Table 1.

When the cancer detection rates of 10-core and 12-core biopsies were compared according to levels of PSA, the rates were 13.1% (5/38) and 15.7% (3/19) in PSA levels of 2.5 to 4.0 ng/mL, 22.8% (50/219) and 21.6% (16/74) in levels of 4.1 to 10.0 ng/mL, and 40.4% (38/94) and 53.3% (16/30) in PSA levels of 10.1 to 20.0 ng/mL. Prostate cancer detection rates showed no statistically significant differences according to PSA levels in 10-core and 12-core biopsy groups (*P* = .540 and *P* = .484, respectively).

When the cancer detection rates of 10-core and 12-core biopsies were compared according to the PV, PCa detection rates were 34.1% (68/199) and 30.0% (18/60) in PV < 40 mL (*P* = .331) and 16.4% (25/152) and 26.9% (17/63) in PV ≥ 40

Table 3. Major complication rates between 10-core and 12-core prostate biopsies.

	Total	10-core prostate biopsy	12-core prostate biopsy	*P*
Hematuria	142 (30%)	102 (29.0%)	40 (32.5%)	.865
Acute prostatitis[a]	10 (2.0%)	7 (1.9%)	3 (2.4%)	.798
Rectal bleeding	5 (1.0%)	4 (1.1%)	1 (0.8%)	.358
Vasovagal syncope	3 (0.6%)	1 (0.2%)	2 (1.6%)	.732
Acute urinary retention[b]	0 (0%)	0 (0%)	0 (0%)	-

[a] Fever > 37.5 ºC and white blood cells/high power field in urine analysis > 4

[b] Residual urine volume > 200 mL

mL (P = .049), respectively.

The PCa detection rates using 10-core and 12-core biopsy scheme according to PSA levels and PV are listed in Table 2.

Of 474 patients, 33.7% (160/474) experienced prostate biopsy-related complications. The most common complication was mild hematuria (30%; 142/474), which was cured without additional treatments. Other complications were acute prostatitis (2.0%; 10/474), rectal bleeding (1.0%; 5/474), and vasovagal syncope (0.6%; 3/474). Complication rates of 10-core and 12-core prostate biopsies were 32.4% (114/351) and 37.3% (46/123). The complication rates are listed in Table 3.

DISCUSSION

With the increased concern of PCa and the wide spread use of serum PSA test, performing prostate biopsy for the detection of the PCa is increasing. Due to the low sensitivity of PSA testing, age-independent markers of the presence, nature, and progression of the PCa are needed to facilitate timely diagnosis and treatment. Recently, metabolomics or metabonomics have been proposed as a novel method of PCa detection. But these methods are still under study and most of countries are using PSA as the screening of the PCa.

The estimated cancer detection rate in Korean men 55 years or older is 3.36%.[6] Among all cancers, the incidence of PCa increased most in Korea. Since Hodge and colleagues first introduced 6-core prostate biopsy,[1] it has been the most widely used method for diagnosing PCa. Several studies reported that the PCa detection rates of 6-core prostate biopsy is approximately 25% to 30%, but it can miss 20% to 30% of PCa detections because of not considering the PV and location of tumor.[7,8]

Many studies attempted to improve the PCa detection rates by increasing the number of biopsy samples using 8-core,[9] 10-core,[10] and 12-core biopsy.[11,12] These extended prostate biopsies improved PCa detection rates and the complication rates were comparable to conventional 6-core biopsy. Presti and colleagues[13] and Moon and associates[10] reported that the 10-core biopsy regimen improved the PCa detection rate by 14% and 23.4%, respectively. Durkan and coworkers reported that the 12-core biopsy improved PCa detection rates up to 19%.[14] Rochester and associates reported that PCa detection rates improved in 12-core and 15-core biopsy groups when compared with conventional 6-core biopsy group.[15]

In studies that compared the 6-core biopsy group with the extended biopsy group, Naughton and coworkers reported that the PCa detection rate in the 6-core and 12-core biopsy groups was 26% and 27%, respectively.[16] Bae and Chang reported that the prostate detection rates of 6-core and 12-core biopsy were 26.8% and 29.2% among patients who were suspected to have T1c PCa. They

stated that 12-core biopsy was not beneficial to improve the cancer detection rates in suspicious T1c PCa.[12]

Several recent studies have examined the cancer detection rates with saturation biopsy. Lane and colleagues found a detection rate of 43% in men who had 20 or more biopsies. The false-negative rate for saturation biopsy was the same as that found with traditional prostate biopsy.[17] Pepe and Aragona found a detection rate of 46.9% for PCa in men who were biopsied with 24 to 37 cores in a saturation technique. A retrospective comparison with 12- and 18-core biopsies in their institution showed comparable detection rates of 39.8% and 49%, respectively.[18]

Our study was different from many other previous studies that compared the 6-core biopsy regimen with the extended biopsy protocols. Our aim was to evaluate the PCa detection rates in extended prostate biopsies (10-core and 12-core biopsies) and assess the benefit of additional two more biopsies in PCa detection. Our results showed that the rate of PCa detection rates of the 10-core and 12-core biopsies were 26.4% and 28.4%, respectively. Performing additional two more biopsies to the 10-core biopsy protocol did not improve PCa detection rate. Limitation of our study is that we excluded conventional 6-core biopsy and compared its detection rate only with extended prostate biopsy.

In many urologic clinics, PSA > 4.0 ng/mL is considered to the standard cutoff value of prostate biopsy. The PCa Prevention Trial (PCPT) recommended performing prostate biopsy even if patients' PSA is less than 4.0 ng/mL with normal DRE findings because 15% of PCa was detected in these patients. Catalona and colleagues reported that in patients whose PSA level was 2.5 to 4.0 ng/mL, the PCa detection rate was 22.0%, and if the cutoff value of PSA was 4.0 ng/mL, approximately 20.0% of patients with the PCa might be overlooked.[19] In patients with increased PSA level to 2.5 to 20.0 ng/mL, we divided patients according to PSA level (2.5 to 4.0 ng/mL, 4.1 to 10.0 ng/mL, and 10.1 to 20.0 ng/mL) and compared 10-core with 12-core prostate biopsy. We found that PCa detection rates improved with the increase of the PSA levels, but no statistical differences were observed in 10-core and 12-core prostate biopsies according to the PSA levels.

Prostate size plays an important role in the diagnosis of PCa, because it correlates directly with the relative amount of tissue sampled per biopsy core.[20] Prostate cancer detection rate is known to be related to the PV, varying from 39% in small glands to 10% in large prostates. But the impact of PV on the prostate biopsy in detecting PCa is still controversial.[12,16] Several researchers have reported that PCa detection rates decrease with increasing the PV. Uzzo and colleagues considered the PV of 50 mL as cutoff[21] and Mariappan and associates considered 40 mL as the cutoff and reported that the PCa detection rates were significantly higher in the small PV.[22]

We defined the large PV as ≥ 40 mL because our indication for surgery was PV over 40 mL that did not respond to medical treatment. In our results, the PCa detection rate of the small PV (< 40 mL) group (33.2%) was higher than large PV (≥ 40 mL) group (19.5%). Comparing the 10-core and 12-core biopsies according to the PV, large PV group improved PCa detection rate in 12-core biopsy. In small PV group, PCa detection rates of 10-core and 12-core biopsies showed no differences (34.1% versus 30.0%). But in large PV group, 12-core biopsy group showed higher PCa detection rates compared with 10-core biopsy group (26.9% versus 16.4%). We think that in patients with large PV (≥ 40 mL), two more biopsies in addition to 10-core biopsy can help improve the PCa detection rate.

In many centers in Korea, prostate biopsy is done on outpatient basis, but some centers prefer to practice biopsy with hospitalized patients.

The reason why we hospitalized the patients is to check and prevent severe complications after the prostate biopsy. With the increase of the number of biopsy samples, the rates of complications, such as hematuria, rectal bleeding, and infection, may be increased. But complications after the prostate biopsy are usually minor.[23] In our results, mild hematuria was the most common complication after the prostate biopsy, but special treatments were not required in most of the patients. The complication rate of hematuria, acute prostatitis, rectal bleeding, and vasovagal syncope in 10-core and 12-core prostate biopsies showed no differences. Since 10-core and 12-core biopsies yielded similar complication rate without statistical differences, we could perform 2 more additional biopsies without worrying about an increase in complication rate with increased samplings.

CONCLUSION

Patients with elevated serum level of PSA to 2.5 to 20.0 ng/mL showed no differences in PCa detection rates of 10-core and 12-core extended prostate biopsy. In patients with large PV (≥ 40 mL), 12-core prostate biopsy is thought to be of help to improve the PCa detection rates. With regard to the cutoff of serum levels of PSA and the PV for the application of extended prostate biopsy, the more prospective studies with larger number of patients are needed in the future.

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CONFLICT OF INTEREST

None declared.

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