Yonsei Medical Journal
Vol. 45, No. 4, pp. 671 - 675, 2004

Can a 12 Core Prostate Biopsy Increase the Detection Rate of Prostate Cancer versus 6 Core?: A Prospective Randomized Study in Korea

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Several studies suggest that standard 6 core sextant transrectal ultrasound (TRUS) guided biopsies of the prostate provides insufficient material to adequately detect clinically important prostate cancer, and that a larger biopsy cores may improve the cancer detection rate. We performed a prospective randomized trial by comparing 6 and 12 core prostate biopsies to determine whether doubling the number of cores in a sextant biopsy improves the prostate cancer detection rate. We randomized 240 men with an elevated serum total prostate specific antigen (PSA) level, abnormal digital rectal examination (DRE) and/or TRUS suspicious for prostate cancer into a 6 core biopsy group and 12 core biopsy group from Jan. 2002 to Jan. 2003. We acquired 3 cores from the right and left prostate lobes for the 6 core biopsy group and three additional cores from each side more peripheral than a 6 core for the 12 core biopsy group. The 6 core and 12 core biopsy groups were well matched with no significant differences in age, prostate volume, PSA and PSA density. The overall cancer detection rate by prostate biopsy was 15.8% (38/240) and the cancer detection rate was not significantly different between the 6 core biopsy group (14.4%, 17/118) and 12 core biopsy group (17.2%, 21/122) (p=0.60). Our study demonstrates no statistically significant improvement in prostate cancer detection rate by increasing the number of biopsy cores. In conclusion, we believe that the standard 6 core sextant biopsy of the prostate is as effective at detecting prostate cancer as a 12 core biopsy in Korean men.

Key Words: Prostate neoplasm, biopsy, ultrasonography

Received May 21, 2004
Accepted July 1, 2004

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INTRODUCTION

The combination of prostate specific antigen (PSA) and transrectal ultrasound (TRUS) of the prostate as screening test for prostate cancer has facilitated the early detection of prostate cancer. Since Hodge et al. first introduced TRUS guided sextant prostate biopsy,[1] it has been the most widely used methods for diagnosing prostate cancer. However, the optimal number of biopsy cores needed to detect prostate cancer remains controversial. Many investigators have reported on this issue and some have insisted that a larger number of biopsy cores should be obtained extensively from the prostate since there is a high possibility of missing a prostate cancer by conventional sextant prostate biopsy.[2-8] On the other hand, others have reported the detection rate of prostate cancer is not significantly increased by taking more biopsy cores.[9-11] Because the standard method of TRUS guided prostate has not been established yet, the majority of urologists have difficulty performing prostate biopsy methodwise. Therefore, we performed a comparative randomized prospective trial of 6 and 12 core prostate biopsies.

MATERIALS AND METHODS

240 consecutive eligible patients who required prostate biopsy at the Yonsei Medical Center from Jan. 2002 to Jan. 2003 were included in this study. The indications for prostate biopsy were 4.0 ng./ml. ≤ PSA < 20.0 ng./ml. and/or a suspicion of

prostate cancer on digital rectal examination (DRE) and/or findings highly suggestive of prostate cancer on TRUS -e.g., a hypoechoic lesion in the peripheral zone.

Patients were randomized into two groups, a 6 core biopsy group and a 12 core biopsy group. Sextant biopsy was performed from the apex, mid, and base of the right and left parasagittal planes of the prostate, and the 12 core biopsy included an additional 3 cores from the peripheral zone positioned more laterally on each side, all under TRUS guidance (Fig. 1). Biopsy was performed either under local anesthesia or general anesthesia and 6 and 12 cores were obtained regardless of prostate volume. In cases under local anesthesia, patients required a 3-5 day administration of fluoroquinolone and midnight NPO from the day before biopsy, and in cases under general anesthesia biopsy was performed as usual followed by a 3-5 day course of antibiotic treatment.

We compared the overall cancer detection rates of the 6 and 12 core biopsies as well as the cancer detection rates of each group when divided into 3 groups according to PSA (PSA < 4.0 ng/ml, 4.0 ng/ml ≤ PSA < 10.0 ng/ml and 10.0 ng/ml ≤ PSA < 20.0 ng/ml), prostate volume (PV < 30 cc, 30 cc ≤ PV < 50 cc and PV ≥ 50 cc) and PSA density (PSAD < 0.10, 0.10 ≤ PSAD < 0.15 and PSAD ≥ 0.15). Statistical analyses of cancer detection rates were performed using Fisher's exact test and comparisons of characteristics of each group were made using the Student's t-test. All p values less than 0.05 were considered significant.

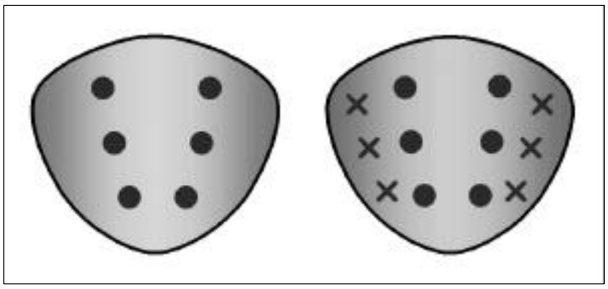

Fig. 1. Transrectal ultrasound guided biopsy of prostate. A, standard sextant biopsy. B, 12 core biopsy, including 6 additional laterally positioned peripheral cores.

RESULTS

118 and 122 patients were included in the 6 core and 12 core biopsy groups, respectively. The patient characteristics of the two groups are as shown in Table 1. Overall mean age, PSA, prostate volume, and PSA density were 62.9 ± 8.7 years, 7.86 ± 3.79 ng./ml., 45.32 ± 19.04 cc and 0.18 ± 0.10 ng./ml./cc, respectively. There were no statistically significant differences in age, PSA level, prostate volume, and PSA density between the two groups (all $p > 0.05$).

Overall cancer detection rate was 15.8% (38/240) and the group specific cancer detection rates were 14.4% (17/118) and 17.2% (21/122) in the 6 core and 12 core groups, respectively, showing no statistically significant difference (p=0.60).

The cancer detection rates in the two groups showed no statistically significant difference even when stratified by PSA level (Table 2), prostate volume (Table 3), and PSA density (Table 4).

DISCUSSION

The screening and early diagnosis of prostate cancer has become increasingly important given

Table 1. Patient Characteristics

	6 cores	12 cores	p value	Overall
Patients No.	118	122		240
Mean age ± S.D.	63.83 ± 6.98	62.00 ± 10.16	0.75	62.91 ± 8.71
Mean PSA ± S.D.	7.51 ± 3.42	8.20 ± 4.15	0.83	7.86 ± 3.79
Mean PSAD ± S.D.	0.17 ± 0.09	0.19 ± 0.11	0.57	0.18 ± 0.10
Mean PV ± S.D.	44.96 ± 19.55	45.79 ± 18.22	0.34	45.32 ± 19.04

PSA, prostatic specific antigen; PSAD, PSA density; PV, prostate volume.

Table 2. Prostate Cancer Detection Rates Stratified by Total PSA

Total PSA (ng./ml.)	No. Pts.	No. Pts./Total No. Pts. (%)		*p* value
		6 cores	12 cores	
4.0 ≤ PSA < 10.0	174	12/93 (12.9)	12/81 (14.8)	0.83
10.0 ≤ PSA < 20.0	66	5/25 (20.0)	9/41 (21.9)	0.85
Total	240	17/118 (14.4)	21/122 (17.2)	0.60

PSA, prostate specific antigen.

Table 3. Prostate Cancer Detection Rates Stratified by Prostate Volume

PV (cc)	No. Pts.	No. Pts./Total No. Pts. (%)		*p* value
		6 cores	12 cores	
PV < 30	34	2/16 (12.5)	4/18 (22.2)	0.66
30 ≤ PV < 50	92	8/48 (16.7)	6/44 (13.6)	0.78
50 ≤ PV	114	7/54 (13.0)	11/60 (18.3)	0.46
Total	240	17/118 (14.4)	21/122 (17.2)	0.60

PV, prostate volume.

Table 4. Prostate Cancer Detection Rates Stratified by PSA Density

PSAD (ng./ml./cc)	No. Pts.	No. Pts./Total No. Pts. (%)		*p* value
		6 cores	12 cores	
PSAD < 0.10	42	3/26 (11.5)	3/16 (18.8)	0.66
0.10 ≤ PSAD < 0.15	92	6/44 (13.6)	6/48 (12.5)	0.87
0.15 ≤ PSAD	106	8/48 (16.7)	12/58 (20.7)	0.63
Total	240	17/118 (14.4)	21/122 (17.2)	0.60

PSAD, Prostate specific antigen density.

the increasing incidence of prostate cancer in the PSA era. The confirmative diagnosis of prostate cancer until now in most institutions mainly depends on the standard sextant TRUS guided biopsy first introduced by Hodge et al., and with a complication rate of less than 1%, this technique can be performed rapidly, safely and easily in most patients.[1,13]

However, questions as to whether the number of cores used in the standard sextant prostate biopsy is sufficient in detecting prostate cancer have arisen and many studies have been undertaken on this subject. Keetch et al. reported a 20% increase in the cancer detection rate after performing serial sextant biopsies, and concluded that sextant biopsy is insufficient for the detection prostate cancer.[2] Eskew et al. reported a 40% cancer detection rate using a systematic 5 region biopsy protocol, when then introduced additional biopsy cores at the midline of the prostate, and at the lateral mid gland they found that 35% of cancers detected were missed by conventional sextant biopsy.[3] Other studies have also reported positive results for extended prostate biopsies and have also emphasized that a greater the number of biopsy cores should be acquired, especially

from the more lateral area of the prostate gland rather than from the parasagittal plane.[4-8]

On the other hand, other reports found no significant difference in the cancer detection rate using extended prostate biopsy. Nava et al. compared the cancer detection rate between, 6, 12 and 18 core biopsies, and obtained cancer detection rates of 15%, 17% and 32%, respectively, showing no significant improvement in cancer detection rate despite increasing the number of cores from 6 to 12 cores, however, the 18 core prostate biopsy showed a statistically significant increase.[9] In a randomized study of 244 patients that received 6 and 12 core biopsies, Naughton et al. reported cancer detection rates of 26% and 27%, respectively and concluded that the 6 core biopsy is sufficient for detecting prostate cancer.[10] Other studies have also supported the futility of increasing the number of cores in terms of increasing the cancer detection rate.[11]

To our knowledge, although the trend is toward extended biopsy -especially 12 core biopsy, controversy remains concerning the standard method of TRUS guided biopsy.

The relation between a higher cancer detection and a greater number of biopsy cores may seem obvious. Stricker et al. demonstrated a correlation between the percent volume of a prostate cancer within a prostate gland and the probability of a positive biopsy using a mathematical model based on Bayes' theorem of conditional probability, and proved that an increase in the number of biopsy cores increases the probability of detecting prostate cancer.[12] However, in spite of this general and practical conclusion, in the present study we obtained cancer detection rates of 14.4% and 17.2% in the 6 core and 12 core groups, respectively, which is a trivial difference that is not statistically significant. Moreover, clinical parameters such as PSA level, prostate volume, and PSA density were not found to have a significant influence on the cancer detection rate. In agreement with our findings, Ung et al. reported in a series involving different core biopsies in different prostate volumes, that the increase in cancer detection rate, regardless of prostate volume, was insignificant even in when the number of biopsy cores was increased up 18, which in their study showed no significant difference from the cancer detection rate obtained by 6 core biopsy.[11]

How can such phenomena be explained? The study of Naughton et al. might offer an explanation.[10] They theorized the presence of a plateau zone in cancer detection when the number of biopsy cores is increased from 6 to 12, and thus drew the conclusion that doubling the number of sextant cores may not affect the cancer detection rate due to the small tumor size, and we are in accord with this conclusion. Hence, though it is evident that increasing the number of prostate biopsy cores will eventually increase the cancer detection rate, it is apparent that in practical terms no real advantage is gained by a 12 core biopsy as opposed to a 6 core biopsy.

Of course the sextant biopsy we performed might differ from that used during the early days. It is generally accepted that a prostate biopsy taken from a more lateral portion of the prostate gland which is more likely to include peripheral zone where prostate cancer mainly develops yields higher cancer detection rates than early sextant biopsies.[14] Moreover, our sextant biopsy might have been performed from a more lateral area of the prostate gland than conventional sextant biopsy. However, we believe that this is unlikely to alter the validity of the result obtained, namely, that increasing the number of biopsy cores does not increase the cancer detection rate. In addition, the overall cancer detection rate in our study was 15.8%, which is lower than that reported by other. This can possibly be explained by the relationship between the prevalence of prostate cancer and race. Although PSA in Korean men is lower than that of Western men,[15,16] most Korean institutes consider the cut off value of abnormal PSA as 4.0 ng./ml. and in spite of the dramatic increase in prevalence of prostate cancer in Korean men which is now 10 per 100,000, it is still far less than that of white American's which is at 110 per 100,000.[17,18] These factors certainly contribute to our lower cancer detection rate, which is not exceptional. In addition, the cancer detection rates of prostate biopsy at other institutions in Korea does not actually differ much from ours, though unpublished which again supports the cancer detection rates of the current study.

Although a nomogram of prostate cancer in a large Korean cohort which can define the rela-

tionship between PSA level and prostate cancer should be performed, we suggest that the characteristics of prostate cancer in Korean men may differ from that of Western men.

In summary, our data demonstrate no statistically significant improvement in the prostate cancer detection rate by increasing the number of biopsy cores. We believe that sextant biopsy of the prostate is as effective at detecting prostate cancer as a 12 core biopsy. However, our randomized study was based on findings in only 240 patients and thus is probably insufficient draw a definite conclusion. Thus, a prospective randomized study of a larger number of Korean men should be performed.

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