ORIGINAL ARTICLE

Nine and twelve specimens from prostate biopsy and their impact on cancer detection: a comparative study

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ABSTRACT

Objective: To demonstrate whether a higher number of biopsy specimens increases prostate cancer detection.

Methods: A retrospective study including 149 patients from whom 9 prostate biopsy specimens were taken in 2007 and 166 patients from whom 12 prostate biopsy specimens were taken in 2008 was carried out. Cancer detection frequency was compared in both groups and results were correlated with prostate specific antigen, digital rectal examination, prostate specific antigen density, and biopsy series number.

Results: Cancer frequency detection was 16.78% with 9 specimens and increased to 29.52% with 12 specimens (*P*= 0.009). There was no significant difference in mean age, prostate specific antigen, prostate volume, and prostate specific antigen density between the two groups. There was no significant increase in cancer detection in either group upon carrying out two or more biopsy series (0% in the 9 specimen group and 5% in the 12 specimen group).

Conclusions: Prostate cancer detection frequency increased significantly when there was an increase from 9 to 12 biopsy specimens. The majority of cases were detected in the first biopsy series.

RESUMEN

Objetivo: Comprobar si el mayor número de fragmentos incrementa la detección del cáncer de próstata.

Métodos: Estudio retrospectivo que incluyó 149 pacientes a los que se les tomaron nueve fragmentos en la biopsia prostática en 2007 y a 166 pacientes, a los que se les tomaron 12 fragmentos en 2008. Se comparó la frecuencia de detección de detección en ambos grupos, correlacionándose los resultados con el APE, el tacto rectal, la densidad del APE y el número de serie de biopsia.

Resultados: La frecuencia de detección de cáncer fue de 16.78% con nueve fragmentos y se incrementó a 29.52%, con 12 fragmentos (p = 0.009). No hubo diferencia significativa en la edad, APE, volumen prostático y densidad del APE promedios entre los dos grupos. En ninguno de los dos grupos se aumento de forma significativa la detección de cáncer al realizar dos o más series de biopsias (0% grupo de nueve y 5% grupo de 12).

Conclusiones: La frecuencia de detección de cáncer de próstata se incrementó de manera significativa al aumentar la biopsias de nueve a 12 fragmentos. Casi todos los casos fueron detectados en la primera serie de biopsias.

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Key words: Prostate cancer, detection, prostate biopsy, Mexico.

Palabras clave: Cáncer de próstata, detección, biopsia prostática, México.

INTRODUCTION

Since the beginning of the era of prostate specific antigen (PSA), many modifications in prostate biopsy techniques and indications have been made for the purpose of improving cancer detection frequency and reducing the number of unnecessary biopsies and secondary complications. One of the general indications for prostate biopsy is a PSA value above 4 ng/mL. Studies with this cut-off point for biopsy indication came out in 1991.[1] In 1992 prostate cancer (CaP) detection frequency in these patients was 5.5%.[2] Data from other more recent studies suggested a detection frequency of 20-30% in patients with PSA between 4 ng/mL and 10 ng/mL[1,3] and therefore PSA above 4 ng/mL was established as biopsy indication cut-off point.

Abnormal digital rectal examination (DRE) is an absolute indication for prostate biopsy. In 1998, Schroder et al reported on the low predictive value of DRE in regard to detection and recommended its replacement by a more sensitive test.[4] However, Carvajal et al suggested that DRE should be used in patients with low PSA since cancer will be detected in initial biopsy in 14-30% of patients with PSA between 1 ng/mL and 4 ng/mL with suspicious DRE.[5] Routine DRE as PSA complement is recommended because aggressive CaP can have low PSA values.

Prostate specific antigen density (PSAD) is obtained dividing PSA value by prostate volume in cm^3 which gives the relation of PSA quantity to prostate tissue quantity.

It is believed that PSAD improves PSA specificity because there is a greater possibility that an increase in PSA is due to cancer when there is an increase in PSAD. Reaman determined that normal density for men with PSA between 4 ng/mL and 10 ng/ml should be under 0.15 ng/mL.[6]

The sextant technique introduced by Hodge in 1989 has been the standard technique for performing prostate biopsy.[7] It is carried out by taking 6 bilateral samples from the base, middle region and apex of the prostate and has a 30% false negative rate.[8]

Many studies have shown that by increasing the number of samples there is a greater CaP detection rate.[8-12] However, a study by Naughton did not demonstrate this phenomenon.[13] Five-region prostate biopsy reduces false negative frequency by 35%. Eighty-eight percent of cancers additionally detected with this technique are found in the lateral regions of the prostate.[14] The performing of two consecutive sextants (one in each lobe) was studied by Levine and resulted in a 30% increase in CaP detection with the additional sextant.[8] Babaian studied the 11-core biopsy method that includes traditional sextant plus one lateral per lobe and another at the midline and bilateral transition zones. In this study there was a 33% increase in CaP detection.[11]

Stewart utilized the 18-45 (mean 23) sample saturation technique to evaluate patients that had previously undergone 6-sample biopsy and that continued to be indicated for biopsy. [10] Only 34% of patients with previous negative biopsy were seen to have cancer with this technique, while 38% of patients with previous negative biopsy were seen to have CaP with the 5-region technique. [15]

The present study evaluates results of the current 12-sample technique compared with the 9-sample technique.

OBJECTIVE

The purpose of the present study is to demonstrate whether a greater number of biopsy samples increases CaP detection, to compare PSA values with biopsy result, and to compare positive DRE results with prostate biopsy positivity in patients from the authors' institution.

METHODS

An observational retrolective cross-sectional study with comparative analysis of CaP detection according to number of samples taken by means of transrectal

Table 1. General patient characteristics.

Group	1	2
Number of samples	9	12
Number of patients	148	166
Age*	68	66
PSA (ng/mL)*	32.8	33.6
Prostate volume*	59.8	63.8
PSAD*	0.69	0.76

*Means

Table 2. Detection percentage per group.

Result	Group 1	Group 2	TOTAL
Positive	25 (16.9%)	49 (29.5%)	74 (23.5%)
Negative	123 (83.1%)	117 (70.5%)	240 (76.5%)
TOTAL	148 (100%)	166 (100%)	314 (100%)

ultrasound-guided prostate biopsy (TRUS) was carried out. The cases records of patients having undergone TRUS in the authors' institution in 2007 and 2008 were reviewed. Patients with incomplete case records and who had a different number of samples taken from that required for the study, were excluded. Nine-sample prostate biopsy was done during 2007 and 12-sample biopsy during 2008. Patients were divided into two groups according to number of samples taken: Group 1 was the 9-sample group and Group 2 the 12-sample group. Biopsy indications used were positive DRE and PSA above 10 ng/mL. Biopsy was indicated in patients with PSA between 4 ng/mL and 10 ng/mL, if free PSA was less than 20%.

Prostate biopsy procedure was carried out in all patients by means of local anesthesia with 2% lidocaine, mechanical intestinal preparation the day prior to procedure, and antibiotic prophylaxis with ciprofloxacin three days before and after biopsy. Patients were instructed not to take aspirin or platelet antiaggregants at least 5 days prior to biopsy. Aloka Pro Sound SSD-4000 Plus equipment with intracavitary transducer ultrasound (US) was used. Total prostate volume was initially measured and PSAD was calculated using total PSA quotient and prostate volume estimated by US.

Nine-specimen technique was carried out by taking nine samples from the peripheral zone of the prostate: at the apex, center and base of the prostate on both the right and left sides and middle sections. Each sample was placed in a test tube with eosin-formol and separately labeled. Twelve-specimen technique was carried out at the same sites as the nine-sample technique and three addition peripheral samples from suspicious zones (hypoechogenic in US) were added.

The following variables were evaluated: age, PSA, prostate volume determined by transrectal US, PSAD, and DRE. Variables were correlated with number of samples and histopathological result.

Analyses were made using descriptive statistics and measures of central tendency and dispersion. Chi-square test, McNemar's test, and Fisher exact test were used for comparative statistical analysis and there was statistical significance when $P < 0.05$. Statistical calculations were carried out using *Windows Stata/SE Ver 9.1, StataCorp LP*, software package.

The Research and Ethics Committee of the author's institution approved the present study.

RESULTS

A total of 350 patients having undergone TRUS in the years 2007 and 2008 were identified. Thirty-six of those patients were excluded from the study due to incomplete case record or due to different biopsy sample number from that needed for the study. A total of 314 patients were included in the study; 148 in Group 1 (9 samples) and 166 in Group 2 (12 samples). Descriptive analysis showed the two groups were homogeneous in reference to age, PSA, prostate volume, PSAD, and initial biopsy percentage (**Table 1**).

The observed detection frequency was 16.8% for Group1 and 29.5% for Group 2, $P = 0.009$ (**Table 2**).

Analysis of DRE and histopathological result correlation showed that patients with abnormal DRE had a higher detection rate if they had had 12-sample biopsy, $P=0.007$ (**Table 3**).

In regard to biopsy series number, there was very low cancer detection in the second series or any higher series number. Only two patients in Group 2 and no patients in Group 1 were in this category (**Table 3**).

In relation to PSA value it was determined that there was greater detection in 12-sample biopsy than in 9-sample biopsy when PSA value was above 4 ng/mL. The highest detection rate was found in patients with PSA above 20 ng/mL (**Table 4**). In regard to PSAD comparison, more cases were detected with 12-sample

Table 3. Detection percentage according to DRE and biopsy series number.

	N° Patients/Total (%)		*p*
	1	2	
N° Biopsy (%)			
First	25/118 (21)	47/129 (36.4)	0.008
Second or higher	0/30 (0)	2/37 (5.4)	0.196
DRE			
Normal	8/94 (8.5)	15/106 (14.4)	0.212
Suspicious	17/54 (31)	34/60 (56.7)	0.007

Table 4. Detection percentage according to total PSA.

	No. Patients /Total (%)		*p*
	1	2	
APE (ng/mL)			
0 - 2.4	1/6 (16.7)	0/1 (0.0)	0.423
2.5 - 4.0	0/4 (0.0)	1 / 2 (50.0)	0.218
4.1 - 10.0	8/74 (10.8)	15/86 (17.4)	0.159
10.1 - 20	3/44 (6.8)	9/47 (19.1)	0.127
over 20	13/21 (61.9)	24/30 (80.0)	0.041
PSAD			
under 0.15	3/60 (5.0)	13/76 (17.1)	0.037
over 0.15	22/89 (24.7)	36/90 (40.0)	0.022

biopsy. The highest number of cases was detected in patients with PSAD above 0.15 (**Table 4**).

There was no statistically significant detection increase in 12-sample biopsy in patients with normal DRE (T1c). The detection rates of clinically undetectable cancer were low in both groups (**Table 5**).

DISCUSSION

Even though today it is common practice to take 10-12 specimens in prostate biopsy there is no consensus as to the ideal sample number. Prostate biopsy procedure is well-tolerated with local anesthesia and has a low complication rate. [16-17] Therefore it is a quick, safe, and relatively easy technique for detecting CaP.

According to the prospective non-randomized studies of Naughton and Levine, there was a 35%[18] and 37%[19] detection rate increase when 12-sample biopsy was carried out as opposed to 6-sample biopsy which had been the standard technique some years ago. No studies in the current literature comparing cancer frequency in relation to 9-sample and 12-sample biopsy were found.

A significant increase in cancer detection with 12-sample biopsy was observed in the present study in the patient total, in patients with suspicious DRE and with PSA above 4 ng/mL.

In the group comparison with respect to PSA value, practically no cancer cases with values under 4 ng/mL were detected because biopsy was not indicated for patients with those PSA values. There was an increase in cancer detection with 12-sample biopsy in all patients with PSA above 4 ng/mL even though results were not statistically significant. In the group of patients with PSA above 20 ng/mL there was a detection rate of 62% with 9-sample biopsy and 80% with 12-sample biopsy. This indicates that there is a big possibility that when PSA values are above 20 ng/mL, cancer is the cause. This is not the case when PSA values are under 20 ng/mL, where detection rates were below 20%.

PSAD analysis showed that the majority of detected CaP patients (24% in Group 1 and 40% in Group 2) had densities above 0.15 ng/mL, which concurs with the information in literature. A statistically significant detection increase with 12-sample biopsy was observed in patients with PSAD lower than 0.15 ng/mL as well as in patients with PSAD above 0.15 ng/mL. This indicates the importance of increasing biopsy sample number in patients regardless of prostate or tumor volume.

It was significant to find such low detection rates in patients with normal DRE (T1c) and PSA under 20 ng/mL. Presently this group of patients is targeted for screening because they are considered to be ideal radical prostatectomy candidates. This suggests that there is still no ideal screening method for detecting CaP since with current methods it is necessary to biopsy many patients in order to detect a few curable cases, many of which are not even clinically significant.

Today prostate biopsy continues to be the best method for detecting CaP despite its disadvantages and weaknesses and therefore CaP diagnosis and treatment continue to be a challenge for the urologist.

Table 5. Detection percentage in patients with normal DRE (T1c).

	No. Patients/Total (%)		*p*
	1	2	
PSA (ng/mL)			
4.1-10.0	4/48 (8.3)	9/57 (15.8)	0.306
10.1-20	0/31 (0.0)	3/33 (9.1)	0.096

CONCLUSIONS

Prostate cancer detection rate increased significantly by increasing number of biopsy samples from nine to twelve.

The greatest probability of detecting cancer is in patients with suspicious DRE and PSA above 20 ng/mL.

Prostate cancer detection frequency in patients that are ideal candidates for curative radical prostatectomy according to current criteria (PSA between 4 ng/mL and 20 ng/mL and normal DRE) was low, regardless of number of samples taken.

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