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Frequency of Adenocarcinoma in Transrectal Ultrasound-guided Prostate Needle Biopsies in Men with Clinical Suspicion of Prostate Cancer and Raised Serum Prostate Specific Antigen

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Abstract

Background: A transrectal ultrasound-guided prostate biopsy is currently the gold standard procedure to detect prostatic adenocarcinoma. There is little information on the clinical utility of this technique for the detection of prostate adenocarcinoma in men with suspected prostate cancer in Pakistan. This study seeks to determine the frequency of prostatic adenocarcinoma by using a transrectal ultrasound-guided octant prostate needle biopsy protocol in men with clinical suspicion of cancer.

Methods: All adult men, aged ≥40 years that consecutively presented with signs and symptoms of prostatism, an abnormal digital rectal examination and/or elevated serum total prostate specific antigen levels at Sindh Institute of Urology and Transplantation, Karachi, Pakistan from March 2011 to February 2012, and who underwent transrectal ultrasound-guided biopsies were included. In most patients, eight cores were taken per case. Each core was separately labeled and processed for histopathological evaluation.

Results: A total of 203 men underwent transrectal ultrasound-guided prostate biopsies during the study period. The mean age of all patients was 65.7±9.3 years. The median serum total prostate specific antigen level was 21.6 ng/ml. The overall frequency of detection of prostate adenocarcinoma in this cohort was 48.8% (99/203). The mean number of positive cores per case was 6.02±2.25; the minimum was one and the maximum, eight.

Conclusion: This study showed a similar detection rate for prostate cancer to that reported in studies from Asian and Western countries. The detection rate was markedly higher compared to a few local studies, which showed a very low incidence because of the unavailability of transrectal ultrasound-guided needle biopsies and lack of prostate specific antigen screening programs.

Keywords: Men, Octant biopsy scheme, Pakistan, Prostatic adenocarcinoma, Prostatism

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Introduction

Adenocarcinoma of the prostate represents the most common form of cancer in adult males with marked variation in its incidence and prevalence throughout the world.[1] Both racial and regional differences have a great impact on the incidence of prostatic adenocarcinoma. An estimated 241,740 new cases of prostate adenocarcinoma were likely to occur in the United States alone in 2012, accounting for 29% of all new cancer cases. An estimated 28170 cases were likely to die of prostate cancer in the United States in 2012, accounting for 9% of all cancer-related deaths.[2] It has been reported that prostate cancer occurs most frequently in African Americans and is rare in Asians in the United States.[3] The age-adjusted incidence rate of prostatic adenocarcinoma is higher in the United States, Canada, Australia, and France, whereas it is low in Asian countries. The mortality rates are higher in Asian countries than in high-risk Western countries.[1]

There is no national population-based data in the literature on the incidence and prevalence of prostate adenocarcinoma in Pakistan. However, a few multicenter, hospital-based and regional tumor registry studies have discussed its prevalence in this population. According to these studies, the incidence of prostate adenocarcinoma is low in Pakistan, estimated at 3.8%. This incidence is most probably attributed to a lower life expectancy and the lack of a screening program.[4] According to the first report from the Karachi Cancer Registry, prostate adenocarcinoma has been ranked as the fifth most common cancer among Pakistani males.[5] It was also the fifth most common malignant tumor in northern areas (6.63%) according to a hospital-based study.[6] The previously reported frequency of adenocarcinoma in transrectal ultrasound (TRUS)-guided prostate needle biopsies has varied from 25.9% to 42% in different studies.[7,8] We have previously reported the presence of prostate adenocarcinoma in 44.4% of TRUS-guided prostate needle biopsies performed out in men with clinical suspicion of prostate cancer.[1] However this study included only 50 patients. The above mentioned studies have included patients with raised serum total prostate specific antigen (PSA) levels associated with or without symptoms of prostatism. Prostate adenocarcinoma rarely causes symptoms until it is advanced, thus its suspicion requires a careful history, physical examination including digital rectal examination (DRE), laboratory investigation including a serum total PSA level, TRUS, and TRUS-guided prostate needle biopsies.[9] The latter is considered the gold standard technique as it has dramatically improved the detection rate of prostate adenocarcinoma.[10,11] A variety of protocols and techniques have been used to achieve high sensitivity for the diagnosis of prostate adenocarcinoma. Hodge et al. recommended systematic sextant biopsies of the prostate in 1989, which were obtained in parasagittal plane halfway between the lateral border and midline of the prostate on the right and left sides from the base, mid gland and apex.[10,12] Later, Stamey et al. recommended shifting biopsies more laterally to adequately sample the anterior horn of the peripheral zone.[13] Presti et al., in 2000, concluded that six systematic biopsies of the peripheral zone were inadequate; a minimum of 8 core biopsies that included the apex, mid-lobar, mid-gland, lateral mid-gland and lateral base should be routinely performed.[7] During the recent past, extended 10-12 core biopsy schemas have been used and advocated by many investigators to be more sensitive in the early diagnosis of prostate adenocarcinoma.[14-19] Unfortunately due to the lack of equipment and technique of TRUS-guided biopsies in developing countries, including Pakistan,[1] extended needle core biopsies have not yet routinely been performed in our center.

This study attempts to determine the frequency of prostate adenocarcinoma in TRUS-guided prostate needle biopsies using the modified octant scheme in Pakistani men with raised serum total PSA levels.

Patients and Methods

This prospective study was carried out at the Department of Histopathology, Sindh Institute of Urology and Transplantation (SIUT), Karachi,

Table 1. The main demographic, laboratory and pathological findings in 203 patients who underwent transrectal ultrasound (TRUS)-guided prostate biopsies.

Variables	Adenocarcinoma n (%)	Benign changes n (%)	Total n	*P*-value
Patients	99 (48.8)	104 (51.2)	203	
Age, mean±SD (years)	67.11±8.9	64.43±9.64	65.7±9.3	
Age, median (years)	67	65	65	
Age groups (years)				
40-50	5 (33.3)	10 (66.7)	15	
51-60	23 (41.8)	32 (58.2)	55	0.278
61-70	43 (51.8)	40 (48.2)	83	
>70 years	28 (56)	22 (44)	50	
PSA*, mean±SD (ng/ml)	524.2±1265.9	20.7±22.78	266.2 ± 917.3	<0.05
PSA, median (ng/ml)	79.9	12.45	21.6	<0.05
PSA levels (ng/ml)				
4-10	6 (17.6)	28 (82.4)	34	
10.01-20	14 (22.6)	48 (77.4)	62	0.001
>20	79 (73.8)	28 (26.2)	107	

*PSA: Prostate specific antigen

Pakistan from March 2011 to February 2012. The study included all consecutive adult males (≥40 years) who presented to the SIUT Prostate Clinic with symptoms of prostatism, elevated serum total PSA levels (≥4 ng/ml) and who underwent TRUS-guided prostate needle biopsies using the modified octant scheme. We recorded their detailed physical examination results, DRE results, and laboratory investigations. The raised serum total PSA values were divided into three arbitrary categories: mild (4-10 ng/ml), moderate (10.01-20 ng/ml) and marked (>20 ng/ml), which were then correlated with the biopsy findings. The study was approved by the institutional ethics review committee and informed consent was obtained from all patients for inclusion in the study.

TRUS-guided biopsy technique

The detailed biopsy technique and procedure were previously reported.[1] Briefly, real-time ultrasound imaging was performed with a Toshiba Nemio 20 ultrasound machine and a 7 MHZ biplanar transrectal probe. TRUS-guided biopsies were obtained in the right or left lateral decubitus position and the prostate was imaged in the sagittal plane. Biopsies were obtained using an automatic biopsy gun (Manan Promag 2.2) and 18 gauge biopsy needle. Frequently in our center, we obtain eight cores that include all major areas of the prostate according to a slight modification of the method used by Presti et al.[7] The ninth core is taken from any suspicious hyper- or hypoechoic area visualized by TRUS examination if not sampled by the standard eight biopsy procedure. In the few cases of a small prostate, we sample less numbers of cores. Each core was individually taken and labeled with the specific site from which it was obtained, in accordance with our protocol.

Pathologic study

All biopsy specimens were fixed in 10% formalin, routinely processed under standardized conditions for paraffin embedding, cut at 3-5 micrometers and stained by hematoxylin and eosin (H&E) for detailed microscopic examination. The histological type of the lesion in each core of the biopsy were determined and recorded separately in the report.

Statistical analysis

The collected data was entered into SPSS (version 10.00) and analyzed. Mean±SD were used for continuous variables such as age and serum PSA levels. Numbers (percentages) were used for categorical data such as the frequency of adenocarcinoma observed in TRUS-guided biopsies.

Table 2. Number of patients, median prostate specific antigen (PSA) values and cancer detection rates according to age ranges.

Age range (years)	Patients n (%)	Median total serum PSA (ng/ml)	Cancer cases n (%)	*P*-value
40-50	15 (7.4)	15.11	5 (33.3)	0.27
51-60	55 (27.1)	19.00	23 (41.8)	
61-70	83 (40.9)	26.6	43 (51.8)	
>70	50 (24.6)	21.5	28 (56)	

For comparison between the prostate cancer and the non-cancer groups, we used the independent sample t- and chi-square tests. A *P*-value of less than 0.05 was considered significant. We stratified patients according to age groups and serum PSA levels to analyze the effects of these modifiers.

Results

A total of 203 men underwent TRUS-guided prostate biopsies during the study period. The mean age of all patients was 65.7±9.3 years with a range of 40 to 92 years; the median age was 65 years. There were 200 patients of 50 years of age or older. The mean serum total PSA level was 266.2±917.3 ng/ml and the range was 4 to 9569 ng/ml. The median serum PSA level was 21.6 ng/ml. In the majority of cases we obtained eight core samples per case. The mean number of cores obtained was 7.36±1.19, with a minimum number of cores per case of 3 and a maximum of 9.

From all patients, 104 (51.2%) had benign changes according to pathologic examinations of the prostate biopsies, whereas 99 (48.8%) had adenocarcinoma of the prostate. The mean number of positive cores per case was 6.02±2.25. The minimum was one and the maximum was eight. The main demographic, laboratory and pathological characteristics of all patients are shown in Table 1.

The relationship between the median serum total PSA level, specific age groups, and cancer detection rate is shown in Table 2. There was an overall increase in cancer detection rate with increasing patient age.

The relationship between the degree of elevated serum total PSA and the cancer detection rate is shown in Table 3. Increased overall cancer detection rate was a function of increased serum total PSA levels.

Discussion

The TRUS-guided prostate needle biopsy procedure is now a well-established technique for early detection of prostate cancer. Several worldwide studies have confirmed its clinical utility. Although elevations of serum total PSA levels and the presence of an abnormal DRE are associated with prostate cancer, these findings lack the specificity for an accurate diagnosis. A variety of tissue procurement procedures are utilized in the detection of prostate cancer, but currently, the TRUS-guided needle biopsy procedure is considered the gold standard method for its detection.

Although we previously reported on the spectrum of pathological lesions in TRUS-guided needle biopsies from SIUT, this was a small scale study of short duration.[1] In comparison, the current study was four times larger and conducted over a one-year period. The focus of this study was to detect the frequency of adenocarcinoma in the schema of TRUS-guided biopsies at SIUT. We believe these results will be more representative of the true frequency of prostate adenocarcinoma in our population. Interestingly, the adenocarcinoma detection rate in this study was similar to our earlier study. The detection rate was slightly better compared with the previous study. The octant biopsy schema used in both studies was the same. Our cancer detection rates were comparable with numerous worldwide studies.[7,10,13-19] The lower frequencies found in some studies might reflect differences in the study population.[20,21] Of note, the majority of subjects

Table 3. Relationship between serum total prostate specific antigen (PSA) level elevations and prostate cancer detection.

Serum PSA levels (ng/ml)	Total cases n (%)	Cancer cases n (%)	*P*-value
4-10	34 (16.7)	6 (17.6)	<0.05
10.01-20.00	62 (30.5)	14 (22.6)	
>20	107 (52.7)	79 (73.8)	

in the current and previous studies presented with symptoms of prostatism.[1] Few asymptomatic patients were evaluated with the intent of screening. The results of the current study suggested the lack of change in the prevalent practice of prostate cancer detection in our center. More studies have focused on the detection of prostate cancer at an early, asymptomatic stage.[9]

The overall detection rate of prostatic adenocarcinoma in our patients was 48.8%, which was slightly higher than the 44.4% rate found in our previous study.[1] The results of both studies were concordant with previously published studies in other Asian countries. In a study from China, the incidence of cancer in prostate was 36.26%.[20] In a Turkish study, the incidence was 44.5%.[21] However, the rates were markedly higher than those reported from other local studies. An overall cancer detection rate of 14.2% of all prostate specimens, which included prostate chippings, prostatectomy specimens, and TRUS-guided needle biopsies was reported in a large study from Karachi, Pakistan.[8] The cancer detection rate in their needle biopsies was 23%, which was markedly low compared to our current and previous studies. Another local study included only prostate chippings that had been removed by transurethral resection of the prostate (TURP) found cancer in 2% of cases.[22] These discrepancies reflected the type of specimens and number of core biopsies obtained per case. The higher sensitivity of the present schema might be related to the larger volume of cancer in our patients, as shown indirectly by severe elevations of serum total PSA in the majority of cases and a higher prevalence (69.2%) of ≥6 positive cores. We did not systematically analyze the volume of the prostate gland or the cancer in this study, nor have we evaluated detailed histopathological characteristics of the adenocarcinoma of the prostate in our patients. These may constitute a topic for future study in our patients.

The mean age of our patients diagnosed with prostate cancer was concordant with most previously published studies.[1,7,13-19] The incidence of this cancer increases with increasing age. We have also observed a rising incidence of prostate adenocarcinoma with age, however the rise was not statistically significant in the present study. This might be due to the relatively small sample size. The highest cancer incidence among the different age groups was seen in men who were >70 years of age.

The incidence of prostate adenocarcinoma also increases with increases in the serum level of total PSA. The highest incidence of cancer was seen in patients whose total serum PSA levels were >20 ng/ml. This was similar to the results from other studies.[1,7,13-19] The majority of our cases (52%) showed this degree of serum PSA elevation, which confirmed the overall delayed presentation of patients in our clinic.[23] The detection rate of cancer was highest in patients with severe elevations of serum total PSA levels. These observations recapitulated the findings reported in our previous study.[1] Although the increase in serum total PSA levels does not confirm cancer, it may also indicate an inflammatory process in the prostate. In this study, 52.7% of the patients had severe elevations of serum total PSA levels. Of these, 28 (26.2%) were found to have benign lesions with or without prostatitis. This finding was similar to that reported in our previous study.[1]

Conclusion

The detection rate of prostate cancer in our

study by using the current octant TRUS biopsy scheme was similar to that reported in published studies worldwide. The incidence was low in a number of local studies because of the unavailability of TRUS-guided needle biopsies and lack of PSA screening programs in Pakistan. There is a need to create awareness among the general population and health professionals for an early diagnosis of this common form of cancer.

References

1. Barakzai MA, Mubarak M, Kazi JI. Histopathological lesions in transrectal ultrasound guided biopsies of prostate with raised serum prostate specific antigen. *Nephro-Urol Mon* 2011;3(3):186-90.
2. Siegal R, Naishaham D, Jemal A. Cancer statistics 2012. *CA Cancer J Clin* 2012;62:10-29.
3. Epstein JI. The Lower Urinary Tract and Male Genital System. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. Robbins and Cotran pathologic basis of diseases, 8th ed. Philadelphia: Saunders Elsevier 2004:971-1004.
4. Aziz Z, Sana S, Saeed S, Akram M. Institution based tumor registry from Punjab. Five year data based analysis. *J Pak Med Assoc* 2003;53(8):350-3.
5. Bhurgri Y. Epidemiology of cancers in Karachi (1995-1999). Karachi: Pharmacia & Upjohn, 2001:59-66.
6. Ahmad M, Khan AH, Mansoor A. The pattern of malignant tumors in Northern Pakistan. *J Pak Med Assoc* 1991;41(11):270-3.
7. Presti JC, Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: Results of a prospective clinical trial. *J Urol* 2000;163(1):166-7.
8. Ahmed Z, Muzaffar S. Prostatic carcinoma with emphasis on Gleason's grading. An institution based experience. *J Pak Med Assoc* 2002;52(2):54-6.
9. Shariat SF, Roehrborn CG. Using biopsy to detect prostate cancer. *Rev Urol* 2008;10(4):262-80.
10. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol* 1989; 142(1):71-5.
11. Brawer Mk, Lange PH. Prostate specific antigen in the management of prostatic carcinoma. *Urology* 1989; 33 suppl:11-16.
12. Hodge KK, McNeal JE, Stamey TA. Ultrasound guided transrectal core biopsies of the palpable abnormal prostate. *J Urol* 1989;142(1):66-70.
13. Stamey TA. Making the most out of six systematic sextant biopsies. *Urology* 1995;45(1):2-12.
14. Ravery V, Goldblatt L, Royer B, Blanc E, Toublanc M, Boccon-Gibod L. Extensive biopsy protocol improves the detection rate of prostate cancer. *J Urol* 2000;164(2):393-6.
15. Eskew A, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. *J Urol* 1997; 157(1):199-203.
16. Presti JC Jr, O'Dowd GJ, Miller MC, Mattu R, Veltri RW. Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates. Results of a community multi-practice study. *J Urol* 2003;169(1):125-9.
17. Babaian RJ. Extended field prostate biopsy enhances cancer detection. *Urology* 2000;55(4):453-6.
18. Babaian RJ, Toi A, Kamoi K, Troncoso P, Sweet J, Evans R, et al. A comparative analysis of sextant and an extended 11-core multisite directed biopsy strategy. *J Urol* 2000;163(1):152-7.
19. Gore JL, Shariat SF, Miles BJ, Kadmon D, Jiang N, Wheeler TM, et al. Optimal combinations of systematic sextant and laterally directed biopsies for the detection of prostate cancer. *J Urol* 2000;165(5):1554-9.
20. Hua L, Xu B, Cheng G, Qiao D, Feng N, Zhang JX, et al. Prostate cancer detected after introduction of PSA screening. *Surg Practice* 2011;15(1):2-6.
21. Barutcuoglu B, Bozdemir AE, Ertan Y, Kabaroglu C, Tamsel S, Hemkimgil M, et al. Performance of total prostate specific antigen and free prostate specific antigen ratio for screening prostate cancer in Turkish population. *Turkish J Cancer* 2009;39(1):18-24.
22. Khan IA, Nasir M, Akbar M, Khattack ID, Khan AN, Jan A, et al. Carcinoma of prostate in clinically benign enlarged gland. *J Ayub Med Coll Abbottabad* 2008;20(2):90-2.
23. Ahmed Z, Qureshi A, Idrees R, Aftab K. Prostatic carcinoma: A Pakistani perspective. *Asian Pacific J Cancer Prev* 2009;10(2):323-4.