1110-5704
African Journal of Urology

Vol. 9, No. 3, 2003
123-128

A RATIONALE FOR PROSTATE CANCER DETECTION IN A DEVELOPING COUNTRY: COMPARISON OF SCREENING AND CASE FINDING

A.R. EL-NAHAS, H. ABOL-ENEIN, M. ABDEL-KHALEK, A. EL-ASSMY, K. AL-KOHLANY, M. EL-BAZ AND E.I. IBRAHEIM
Mansoura Urology and Nephrology Center, Mansoura, Egypt

Objectives: This study was conducted to compare the results of a community-based screening program for prostate cancer with case findings among urologic patients.

Patients and Methods: Two programs for prostate cancer detection were conducted based on PSA assay (cutoff value 4 ng/ml) and DRE for men aged 50 to 75 years. The first one included 833 urologic patients (Group I) and the second one included 882 men who had responded to a campaign for early detection of prostatic diseases (Group II). The diagnosis of prostatic adenocarcinoma depended on ultrasound-guided six-core prostatic biopsies.

Results: In Group I, 154 patients were biopsied (147 due to high PSA ± suspicious DRE and 7 due to suspicious DRE alone). Prostate cancer was detected in 41.7% of them (15 patients). In Group II, 75 men were biopsied (69 for high PSA ± suspicious DRE and 6 for suspicious DRE alone). The cancer detection rate was 2.2% (19 patients) and the rate of organ-confined disease was 37.87% (7 patients). There was no significant statistical difference between both groups regarding cancer detection rates and the percentage of organ-confined tumors.

Conclusion: The results of this study may present a rationale for the application of a prostate cancer detection program carried out on urologic patients in developing countries.

Key Words: prostate cancer, screening, PSA

INTRODUCTION

Prostate cancer screening remains a source of major controversy. Potential benefits include the early detection of organ-confined tumors because the prognosis of prostate cancer is related principally to the stage and grade of the disease at the time of diagnosis. The high proportion of clinically localized prostate cancer when detected by screening coupled with the high disease-specific survival rates after radical prostatectomy, forms the basis for recommendation of mass screening for prostate cancer[1,2].

Furthermore, a decrease of prostate cancer mortality rates below the levels that existed prior to the introduction of PSA-based screening has been observed. This decrease has been pronounced in areas where screening is prevalent.[3,4]

On the other hand, critics to mass screening programs have raised concerns regarding the possibility of over-detecting clinically insignificant tumors and lead time bias. This means that the natural history of the disease is not truly affected by screening because of detection and aggressive treatment of biologically indolent tumors that would otherwise remain harmless[5,6]. This was proved by the observation of the 10-year disease-specific survival in patients with clinically localized grade I or grade II prostate cancer which was quite good with conservative management. Moreover, the treatment of prostate cancer has the potential risk of developing urinary incontinence and erectile dysfunction with an estimated mortality rate of 0.5%[8,9]. The last concern is the high cost of screening, which is very important especially in developing countries. It includes the costs of detection, treatment and management of related complications[10]. The potential bene

Table 1: Age Interval, PSA Interval and DRE

	Urologic Group		Community Group	
	No.	%	No.	%
Age interval:				
50 – 59 years	405	48.6%	491	55.7%
60 - 69 years	294	35.3%	292	33.1%
70 – 75 years	134	16.1%	99	11.2%
PSA Interval:				
<4	686	82.4%	813	92.2%
>4	147	17.6%	69	7.8%
DRE:				
- Free	288	34.6%	464	52.6%
- BPH	462	55.5%	369	41.8%
- Suspicious for prostate cancer	32	3.8%	19	2.2%
- Bladder tumor	4	0.5%	2	0.2%
- Small prostate	47	5.6%	28	3.2%

fits and harms of prostate cancer screening continue to be debated among health professionals, and the validity of a community based screening is still questionable.

This study was conducted to compare the results of a community based screening program with case findings among urologic patients attending Mansoura Urology and Nephrology Center in Egypt. The comparison included the detection rates and the tumor characteristics of the diagnosed cases.

PATIENTS AND METHODS

Two programs for prostate cancer detection were carried out at Mansoura Urology and Nephrology Center. The first was conducted between February 1997 and February 1999 when 833 men who were seeking medical advice for urologic disorders were screened for prostate cancer (Group I). The second program was conducted between February and July 2001, where 882 men responded to a campaign for early detection of prostatic diseases (Group II). Both groups included males aged between 50 and 75 years who had not been previously diagnosed to have prostate cancer. The screening tests were digital rectal examination (DRE) and total serum PSA assay [IM total PSA assay (Abbot laboratories, USA) (Cutoff value 4 ng/ml)]. Transrectal ultrasound guided six-core prostatic biopsies were indicated in men with PSA $\geq$ 4 ng/ml and or suspected prostate cancer on DRE. Biopsies from palpable pro-static nodules or hypoechoic areas were also obtained.

Blood samples for PSA assay were obtained prior to rectal examination or after 6 weeks, if the patient underwent urethrocystoscopy or active prostatic infection was suspected. When prostatic adenocarcinoma was diagnosed, staging of the tumor was completed using clinical, radiologic (CT or MRI and bone scan) and histopathologic characters (Gleason score, number and distribution of positive cores). Treatment depended on tumor stage and medical fitness of the patient. The patients' and tumors' characteristics of both groups were compared using chi-square test.

Table 2: Relative Sensitivity (RS) and Positive Predictive Value (PPV)

	Group I				Group II			
	Relative Sensitivity*		Pos. Predictive Value+		Relative Sensitivity*		Pos. Predictive Value+	
	No.	%	No.	%	No.	%	No.	%
PSA	33/36	91.7%	33/147	22.4%	16/19	84.2%	16/69	33.2%
DRE	17/36	47.2%	17/32	53.1%	9/19	47.4%	9/19	47.4%
(P>0.05)								

* Relative sensitivity: Number of positive tests in those who had cancer detected by biopsy.
+ Positive predictive value: Number of cancers in patients with positive tests

RESULTS

The mean age of the patients was 60.6 ± 7.7 years in Group I and 59.6 ± 7 years in Group II. In Group I, 426 patients (51.1%) had upper urinary complaints and 407 patients (48.9%) had lower urinary complaints. In Group II, 543 men (61.6%) responded to the campaign because they suffered from lower urinary tract symptoms, while 339 men (38.4%) had no complaints.

In the 833 urologic patients of Group I, mean PSA was 3.5 ng/ml ± 7.4 SD. PSA was ≥ 4 ng/ml in 147 patients (17.6%) and a suspicious prostate on DRE was found in 32 patients (3.8%); 25 with high PSA and 7 had a normal PSA level (Table 1). Therefore, prostatic biopsies were obtained from 154 patients (18.5%). Ultrasound images showed hypoechoic nodules in 66 out of 154 patients (42.2%). Prostate adenocarcinoma was diagnosed in 36 of 833 cases (4.3%); 33 of them were suffering from lower urinary tract symptoms (91.7%).

In the 882 men of Group II, mean PSA was 1.8 ng/ml ± 3.5 SD. PSA was ≥ 4 ng/ml in 69 (7.8%) and DRE was suspicious in 19 (2.2%); 13 with high PSA and 6 had normal PSA level. Therefore, prostatic biopsies were carried out for 75 men (8.5%). Prostatic adenocarcinoma was diagnosed in 19 of 882 men (2.2%). All prostate cancer cases were suffering from lower urinary tract symptoms.

The mean age of our prostate cancer cases was 68.2 ± 7.1 years in Group I and 68.53± 7.26 years in Group II. As expected, the PSA test demonstrated the highest relative sensitivity (91.7% in Group I and 84.2% in Group II) but it had the lowest positive predictive values (22.4% in group 1 and 23.2% in group 2). (Table 2).

Low grade tumors (Gleason score < 7) were detected in 41.7% and 42.1% in Groups I and II, respectively. Organ-confined prostate cancer was detected in 15 out of 36 cases in Group I (41.7%). Radical prostatectomy was carried out for 9 of them. In Group II, localized prostate cancer was diagnosed in 7 out of 19 cases (37.8%). Radical prostatectomy was carried out for 4 of them (Table 3). As for the result of the statistical analysis, the difference of cancer detection rates and percentage of organ-confined disease between both groups were not significant.

DISCUSSION

There is now a widespread call to incorporate routine PSA based screening for prostate cancer into the care of men over the age of 50 years. The potential advantages of early detection of prostate cancer is to identify patients with clinically significant disease that have a biologic potential to cause morbidity during his life time which can be controlled with treatment[11]. On the other hand, the potential disadvantages include overdetection and unnecessary treatment of clinically insignificant tumors and the high cost of screening programs[5,6,10].

Results of prostate cancer screening tests such as sensitivity, specificity and predictive values have been previously reported.[12,13] For ethical reasons, we did not biopsy all screened population. Therefore, false negative results,

Table 3: Prostate Cancer Cases

	Urologic Group (n=36)		Community Group (n=19)		P-Value
	No.	%	No.	%	
Stage:					
Localized	15	41.7%	7	37.8%	
Advanced or metastatic	21	58.3%	12	63.2%	P=0.728
Gleason score:					
<7	15	41.7%	8	42.1%	
≥7	21	58.3%	11	57.9%	P=0.972
Treatment:					
Radical	9	25.0%	4	21.1%	
Expectant	2	5.6%	1	5.3%	
Radiopathy	2	5.6%	3	10.5%	
Hormonal	23	63.8%	12	63.2%	P=0.917

sensitivity and specificity cannot be calculated. But the accuracy of the tests can be expressed as relative sensitivity and positive predictive values[14]. PSA remains the best single test for early detection of prostate cancer because of its high sensitivity (80%)[13]. In the present study, 91.7% and 84.2% relative sensitivity for the PSA test in Groups I and II, respectively were detected. Nevertheless, this test had low positive predictive values (22.4% in Group I and 23.2% in Group II). This is because PSA is not cancer specific as it can be elevated with BPH. The results augment the value of utilizing methods to improve PSA sensitivity, such as PSA density, percent of free to total PSA level and increasing PSA cut off values in men over the age of 60 years (age-adjusted PSA levels).

In spite of the high sensitivity of the PSA test, the diagnostic yield is higher when the latter is combined with DRE. Catalona et al. reported 20% of significant prostate cancer diagnosed in men with PSA < 4 ng/ml[15]. In this series, three prostate cancer cases in each group had PSA < 4 ng/ml and were biopsied due to suspicious DRE (8.3% in Group I and 15.8% in Group II).

While Cooner et al. reported cancer detection rates of 14.6% for urologic patients[16] and Smith et al. observed 3.2% in the community[17], the cancer detection rates in our study were lower than what has been reported previously as we observed 4.3% in urologic patients and 2.2% in the community-based screening. The reasons for this might be due to the younger age of our screened population in both groups as the mean age was 60 years while the mean age of prostate cancer patients was 68 years. Another reason may be the low prevalence of prostate cancer in our population although this speculation has not been proved. An important point is that the difference between cancer detection rates in a community and urologic patient screening was not statistically significant.

The value of a screening program is not only the detection of prostate cancer cases, but especially the detection of the disease in an early stage because patients with clinically localized cancer of low grade are considered the best candidates for curative treatment. Organ-confined cancer was detected in 41.7% in Group I and 37.8% in Group II. These percentages are also lower than those of other screening programs[1,17,18] which may be due to the adoption of serial PSA screening protocols in these studies compared to single PSA assay in our study or due to missing some low-volume tumors in our series when depending on six-core prostatic biopsies. Also, the difference in detection of organ-confined disease in both

groups was not statistically significant. Moreover, tumors with low Gleason score (< 7) were detected in 41.7% in Group I and 42.1% in Group II.

In developing countries (as Egypt), we do not have the facilities to screen all men above the age of 50 years because the health care resources are limited. In the present study, the costs of both programs were approximately the same, but in the urologic patient screening the costs were distributed over 2 years while in the community it took only 6 months to complete the program which reflects its higher cost.

When comparing the cancer detection rates and the percentage of localized prostate cancer in urologic patients and community-based screening, we find no statistically significant difference.

In conclusion, in developing countries where the health care resources are limited, prostate cancer detection programs should mainly be applied to urologic patients.

ACKNOWLEDGEMENT

We would like to thank Professor Ahmed Shokeir for his valuable instruction and ideas which were of great help during editing the manuscript.

REFERENCES

1. Crawford ED, De Antoni EP, Etzioni R *et al.* Serum prostate specific antigen and digital rectal examination for early detection of prostate cancer. A national community based program. *Urology* 1996, 47:863-869.

2. Gerber GS, Thisted RA, Scardino PT *et al.* Results of radical prostatectomy in men with clinically localized prostate cancer. *JAMA* 1996, 276:615-619.

3. Greenlee RT, Hill-Harmon MB, Murray T *et al.* Cancer statistics. *CA Cancer J Clin* 2001, 51:15-36.

4. Bartsch G, Horninger W, Klocker H *et al.* Decrease in prostate cancer mortality following introduction of prostate specific antigen (PSA) screening in the federal state of Tyrol, Austria. *J Urol* 2002, 163:88, A 387.

5. Albertsen PC, Hanley JA, Gleason DF *et al.* Competing risk analysis of men aged 55-74 years at diagnosis managed conservatively for clinically localized prostate cancer. *JAMA* 1998, 280:975-980.

6. Porok PC, Connor RJ, Baker SG. Statistical consideration in cancer screening programs. *Urol Clin North Am* 1990, 17:699-708.

7. Lu-Yao GL, Yao SL. Population-based study of long-term survival in patients with clinically localized prostate cancer. *Lancet* 1997, 349:906-910.

8. Fowler FJ Jr, Barry MJ, Lu-Yao GL *et al.* Effect of radical prostatectomy for prostate cancer on patients quality of life: Results from a Medicare survey. *Urology* 1995, 45:1007-1015.

9. Mark DH. Mortality of patients after radical prostatectomy. Analysis of recent Medicare claims. *J Urol* 1994, 152:896-898.

10. Optenberg SA, Thompson IM. Economic of screening for carcinoma of the prostate. *Urol Clin North Am* 1990, 17:719-737.

11. Sarma AV, Schottenfeld D. Prostate cancer incidence, mortality and survival trends in the United States: 1981-2001. *Sem Urol Oncol* 2002, 20:3-9.

12. Crawford ED. Prostate cancer awareness week: September 22 to 28, 1997. *CA Cancer J Clin* 1997, 47:288-296.

13. Brawer MK. Prostate specific antigen. Current status. *Ca Cancer J Clin* 1999, 49:264-281.

14. Schröder FH, Wildhagen MF. Screening for prostate cancer: Evidence and perspectives. *BJU Int* 2001, 88:811-817.

15. Catalona WJ, Smith DS, Ornstein DK. Prostate cancer detection in men with serum PSA concentration of 2.6 to 4 ng/ml and benign prostatic examination: Enhancement of specificity with free PSA measurements. *JAMA* 1997, 277:1452-1455.

16. Cooner WH, Mosley BR, Rutherford CL Jr *et al.* Prostate cancer detection in a clinical urologic practice by ultrasonography, DRE and PSA. *J Urol* 1990, 143:1146-1152.

17. Smith DS, Bullock AD, Catalona WJ *et al.* Radical difference in a prostate cancer screening study. *J Urol* 1996, 156:1366-1369.

18. Murphy GP. Report of the American Urologic Association. American Cancer Society scientific seminar on the detection and treatment of early stage prostate cancer. *CA Cancer J Clin* 1994, 44:91-95.

RESUME

Réflexions à propos de la Détection de Cancer de Prostate dans les Pays en Voie de Développement: Comparaison du Dépistage de Masse et de la Détection chez les Patients Urologiques

Objectif: Cette étude a été entreprise pour comparer les résultats du programme de dépistage de masse du cancer de prostate aux cas diagnostiqués parmi les patients urologiques. **Patients et méthodes**: Deux programmes pour la détection de cancer de prostate ont été conduits basés sur l'analyse de PSA (la valeur cutoff est de 4ng/ml) et DRE pour les hommes a de 50 à 75 ans. Le premier a inclus 833 patients urologiques (le groupe 1) et le deuxième a inclus 882 hommes qui ont répondu à une campagne pour la détection tôt des pathologies prostatiques (groupe 2). Le diagnostic de l'adénocarcinome prostatique dépend des biopsies prostatiques en sextant guidées par ultrasons. **Résultats**: Dans le groupe 1, 154 patients ont été biopsiés (147 pour PSA élevés ± DRE suspect et 7 pour un DRE suspect seul). Le cancer de prostate a été diagnostiqué chez 36 patients (4.3%). Le cancer confiné à l'organe a été détecté dans 41.7% d'entre eux (15 patients). Dans le groupe 2, 75 patients ont été biopsiés (69 pour PSA élevés ± DRE suspect et 6 pour un DRE suspect). Le taux de détection de cancer prostatique était de 2.2% (19 patients) et le taux de maladie confinée à l'organe était 37.87 (7 patients). Il n'y avait aucune différence statistique significative entre les groupes concernant des taux de détection de cancer et les pourcentages des tumeurs confinées à l'organe. **Conclusion**: Les résultats de cette étude peuvent présenter un argument pour l'application du programme de détection de cancer de prostate dans les pays en voie de développement en faveur d'un dépistage sélectif chez les patients urologiques.

All correspondence to be sent to:

El-Housseiny I. Ibraheim
Urology and Nephrology Center
Mansoura University
Mansoura
Egypt