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Comparison of Digital Rectal Examination and Prostate Specific Antigen in Early Detection of Prostate Cancer

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A B S T R A C T

This study compares the value of digital rectal examination (DRE) and prostate specific antigen (PSA) determination in the detection of prostate cancer. 1,000 men aged ≥ 50 from the Osijek surroundings were examined. The subjects with prostatitis were excluded from the study. The subjects with elevated concentration of total prostate specific antigen and/or digital rectal examination suspect of carcinoma underwent prostate biopsy. The rate of prostate cancer detection showed to be 3.3% for PSA > 4 ng/ml, 2% for abnormal finding of DRE, and 3.7% for combination of the two methods. Out of 35 patients with prostate cancer detected, 19 had suspect DRE finding and 32 had PSA exceeding 4 ng/ml. Thus, PSA pointed to the diagnosis of prostate cancer in 91.4%, and abnormal finding of DRE in 54.2% of cases, the difference being statistically significant. The positive predictive value was 48.7% for abnormal finding of DRE, 47% for PSA > 4 ng/ml, and 80.0% for the combination of both. Although PSA determination detected a considerable proportion of tumors missed on DRE, the former alone was found to be insufficient as a screening method because of its inadequate sensitivity. When combined with digital rectal examination, the probability of prostate cancer detection increased considerably.

Key words: *prostate cancer, prostate specific antigen, early detection.*

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Introduction

Prostate cancer is a common disease in men aged ≥ 50[1–3]. It is diagnosed in about 1% of men aged ≥ 50, to rise abruptly in the sixth and seventh decade of life, the highest incidence being recorded in the seventh and eighth decade of life[4]. The prostate cancer mortality rate also increases with age[2,5]. It is so because most cases of prostate cancer are diagnosed when it has already disseminated beyond the gland itself, which is associated with poor prognosis and limited therapeutic success. Therefore, a more favourable approach should obviously include identification and removal of precancerous lesions, or detection of the disease at an early stage (early detection), when successful treatment is still possible[6–11].

In the diagnosis of prostate cancer, the search for a more sensitive and specific tumor marker than acid phosphatase resulted in the discovery of prostate specific antigen (PSA)[12,13]. Now, PSA is the most important tumor marker in the detection of prostate cancer. When compared with digital rectal examination (DRE), the basic examination that the prevention and early diagnosis of prostate cancer had previously relied on, PSA was demonstrated to detect a significant proportion of tumors missed on DRE[2,14–16].

The efficacy of DRE and PSA in the detection of prostate cancer has been evaluated in a number of studies, however, these multicenter studies suffered from some serious shortcomings. Namely, study population was not selected by the same investigator nor examined by use of the same equipment. Therefore, we decided to conduct this study according to an improved study protocol.

Subjects and Methods

During the study, 1000 men aged ≥ 50 from the community of Čepin and village of Josipovac near Osijek were examined. In Josipovac, 297 of 410, and in Čepin 703 of 1050 men aged ≥ 50 were included in the study. Study subjects were recruited by the method of random choice. They were individually invited in writing to enroll in the study, with the respective information being additionally disseminated through mass media (newspapers, radio, TV). The subjects with prostatitis or urinary tract infection were excluded from the study. On examination, study subjects were asked about the possible presence of the following signs or symptoms of prostate disease: hematuria, hematospermia, dysuria, frequency, urgency, slow urine flow, or ostalgia.

Blood samples were collected for determination of total serum prostate specific antigen (PSA). Blood samples for PSA determination were obtained before digital rectal examination (DRE). The same urologist performed all DREs. The subjects with elevated total PSA (> 4 ng/ml) and/or DRE finding suspect of cancer (abnormal DRE), including induration, asymmetry, or irregularity indicative of cancer, were invited in writing to present for prostate biopsy. These subjects underwent 12 transperineal ultrasound-guided needle biopsy procedures (6 tips and 6 bases) for histology and identification of patients with prostate cancer.

Radioimmunologic methods were used for biological material analysis. Total serum PSA concentrations were measured by PSA-RIACT radioimmunoassay (Cis-Biointernacional, France). Mean values were expressed as arithmetic mean (X), and scatter as standard deviation (SD). Partial differences between groups representing quantitative data were tested by *t*-test. Statistical significance was considered at levels of 5% and 1% ($p < 0.05$ and $p < 0.01$).

Results

Subject classification

Classification of study subjects is presented in Table 1. A group of 49 patients with chronic prostatitis were identified on the basis of signs and symptoms characteristic of prostatitis, and increased leukocyte and bacterial count in urinary sediment. Upon exclusion of this group of prostatitis patients, 951 patients remained in the study. In seven patients, prostate cancer had been previously verified on outpatient examination, so that PSA concentration was determined and DRE was performed in 944 patients. Elevated level of total PSA was found in 68, and DRE suspect of prostate cancer in 44 men. Eighty-eight of 944 subjects underwent prostate biopsy, whereas five subjects refused the procedure. Prostate cancer was detected in 35 patients. A group of 225 men with benign prostate hyperplasia (BPH) were identified according to BPH criteria (signs of prostatism, and prostate enlargement on DRE). Elevated PSA level was recorded in 32 BPH patients, in whom prostate cancer was ruled out by prostate biopsy.

The group of healthy subjects consisted of 655 men free from prostatitis, prostate cancer, or BPH, and with normal PSA and DRE.

Comparison of the efficacy of DRE and PSA in detection of prostate cancer

The value of PSA and DRE in the detection of prostate cancer is illustrated in Tables 2–4. Based on these diagnostic methods (abnormal DRE and/or PSA > 4 ng/ml), the existence of prostate cancer was suspected in 93 (9.7%) subjects. Suspect DRE findings were observed in 44, and elevated PSA level in 68 subjects. Prostate biopsy was performed in 88 (9.3%) of 944 subjects, whereas five subjects refused the procedure. Out of 88 subjects submitted to prostate biopsy, suspect DRE was recorded in 39, PSA values exceeding 4 ng/ml in 68, and both abnormal DRE and PSA > 4 ng/ml in 20 subjects. Prostate cancer was detected in 35 (39.7%) of 88 subjects with prostate biopsy. The rate of prostate cancer detection was 3.3% for PSA > 4 ng/ml, 2.0% for abnormal DRE, and 3.7% for the combination of both. Of 35 patients with detected prostate cancer, 19 had suspect

TABLE 1
EPIDEMIOLOGY OF PROSTATE CANCER – CLASSIFICATION OF STUDY SUBJECTS

Subject group	N	%
Healthy subjects	655	65.5
Patients		
Abnormal digital rectal examination without prostate cancer	25	2.5
Elevated PSA without prostate cancer	4	0.4
Prostate cancer – detected on screening	35	3.5
Prostate cancer – outpatients	7	0.7
Benign prostate hyperplasia with elevated PSA	32	3.2
Benign prostate hyperplasia	193	19.3
Chronic prostatitis	49	4.9
Total	1,000	100.0

PSA = prostate-specific antigen

TABLE 2
EARLY DETECTION OF PROSTATE CANCER – RATE (%) OF PROSTATE CANCER DETECTION BY PROSTATE SPECIFIC ANTIGEN (PSA) AND DIGITAL RECTAL EXAMINATION (DRE)

Method of screening	No. of positive findings	No. of biopsy procedures	No. of prostate cancers detected on screening	Rate of detection (%)
Abnormal DRE	44	39	19	2.0
PSA > 4 ng/ml	68	68	32	3.3
Abnormal DRE and/or PSA > 4 ng/ml	93	88	35	3.7

TABLE 3
EARLY DETECTION OF PROSTATE CANCER – COMPARISON OF PROSTATE CANCER PERCENTAGE DETECTED BY PROSTATE SPECIFIC ANTIGEN (PSA) AND DIGITAL RECTAL EXAMINATION (DRE)

Method of screening	No. of prostate cancer	Percentage of prostate cancer
Abnormal DRE	19	54.2
PSA > 4 ng/ml	32	91.4
Abnormal DRE and/or PSA > 4 ng/ml	35	100.0

TABLE 4
EARLY DETECTION OF PROSTATE CANCER – COMPARISON OF PROSTATE CANCER PERCENTAGE DETECTED BY PROSTATE SPECIFIC ANTIGEN (PSA) AND DIGITAL RECTAL EXAMINATION (DRE)

Method of screening	No. of biopsies	No. of prostate cancer	Positive predictive value (%)
Abnormal DRE	39	19	48.7
PSA > 4 ng/ml	68	32	47.0
Abnormal DRE and PSA > 4 ng/ml	20	16	80.0*
Abnormal DRE and/or PSA > 4 ng/ml	88	35	39.7

* Significant at a level of 1%

DRE and 32 had PSA > 4 ng/ml. Thus, elevated PSA pointed to the diagnosis of prostate cancer in 91.4%, and abnormal DRE in 54.2% of cases, the difference being statistically significant. Positive predictive value for abnormal DRE and PSA > 4 ng/ml was 48.7% and 47.0%, respectively. The difference between these two values did not reach statistical significance. Positive predictive value for the combination of abnormal DRE and PSA > 4 ng/ml was 80.0%, which was statistically significantly higher than the abovementioned values.

Discussion

The objective of this prospective controlled study was to compare the efficacy of DRE and serum PSA in the detection of prostate cancer. Results of the study showed that a significantly greater pro-

portion of tumors were detected by use of serum PSA (91.4%) than by DRE (54.2%). These results are comparable to those previously reported from an American study on 82% and 55% of prostate tumors detected by PSA and DRE, respectively[2].

Besides the percentage of detected tumors, positive predictive value is another important parameter in the evaluation of methods for cancer detection, indicating the percentage of true cancer patients when the method of detection has produced a suspect finding. Positive predictive value is the more important as a higher value implies less unnecessary biopsies[2,17]. In our study, positive predictive value for PSA was 47%, and for DRE 48%, the difference between them being no significant. Different findings for positive predictive value have been reported from the above-mentioned American study, i.e. 32% for PSA and 21% for DRE, the difference between the two values being statistically significant[2]. The obvious discrepancy between the results obtained in the two studies could be explained by different approaches and study conditions involved.

For ethical reasons, none of our study subjects with normal DRE and PSA underwent prostate biopsy. Therefore, neither data on false-negative results could be obtained nor the sensitivity and specificity of the methods could be calculated.

The present study produced an excellent rate of cancer detection (3.7%) as compared with other reports. PSA yielded a higher rate of cancer detection (3.3%) than DRE (2.0%). Detection rates reported in the literature range from 1% to 15%[17–19]. As the age distribution of men submitted to screening in these studies was not comparable to our study population, no direct comparison could be made. Similar rates of cancer detection and a 15% rate referring to symptomatic patients have been reported from the multicenter study[2]. The screening performed at Washington University yielded a 7% rate of cancer detection in a younger population of Afro-Americans. For the time being, these results have been attributed to the role played by genetic factors[20].

The results of the present study as well as recent literature reports indicate that PSA detects a significant number of prostate tumors missed on DRE[2,14,21–23]. In spite of this difference in favor of PSA, though, PSA determination alone is insufficient for reliable screening due to its inadequate sensitivity. The probability of successful prostate cancer detection increases when this method is used in combination with DRE, as also suggested by other authors[21–23].

However, several new reports from screening programs, utilizing a lower cut off for PSA, indicate that the value of DRE may be very small and probably not cost-efficient[24]. The decision on whether to carry out DRE depends upon the situation.

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USPOREDBA DIGITOREKTALNOG PREGLEDA I ODREĐIVANJA PROSTATIČNOG SPECIFIČNOG ANTIGENA U RANOM OTKRIVANJU KARCINOMA PROSTATE

S A Ž E T A K

U radu je uspoređena efikasnost digitorektalnog pregleda (DRE) i određivanja koncentracije prostatičnog specifičnog antigena (PSA) u detekciji karcinoma prostate. Tijekom istraživanja pregledano je 1000 muškaraca starijih od 50 godina, iz općine Čepin i sela Josipovac kod Osijeka. Bolesnici s prostatitisom isključeni su iz istraživanja. Ispitanici koji su imali povišenu koncentraciju ukupnog PSA i/ili suspektan DRE, podvrgnuti su biopsiji prostate. Rezultati pokazuju da je stopa detekcije karcinoma prostate iznosila 3.3% za PSA > 4 ng/ml, 2% za abnormalan nalaz digitorektalnog pregleda (Abn DRE) i 3.7 % za kombinaciju obiju metoda. Od 35 bolesnika s otkrivenim karcinomom prostate, 19 je imalo sumnjiv DRE i 32 PSA preko 4 ng/ml. Stoga, PSA vrijednost ukazuje na dijagnozu karcinoma u 91.4% slučajeva, a abnormalan nalaz DRE u 54.2%. Razlika je značajna. Pozitivna prediktivna vrijednost (PPV) za Abn DRE iznosila je 48.7%, a za PSA > 4 ng/ml 47%. PPV za Abn DRE i PSA > 4 ng/ml bila je 80%. Usprkos tome što PSA detektira značajan broj tumora propušten prilikom DRE, nije dostatno određivanje samo PSA u programu probira jer je ta metoda nedostatno osjetljiva da bi se sama koristila. U kombinaciji s DRE povećava se mogućnost otkrivanja karcinoma prostate.