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Original scientific paper

Role of Screening in Detection of Clinically Localized Prostate Cancer

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A B S T R A C T

The aim of this study was to confirm the role of screening by determining the percentage of clinically localized prostate cancer (stage A and B) in patients with prostate cancer detected on screening and in those presenting to urologic clinic for the symptoms of urination impairment or ostalgia. During the study, 1,000 men aged ≥ 50 from the community of Čepin and village of Josipovac near Osijek were examined. The subjects with elevated concentration of total prostate specific antigen and/or digital rectal examination suspect of carcinoma underwent transperineal biopsy of the prostate. Clinical staging was performed in patients with prostate cancer detected on screening, and data on clinical staging for prostate cancer patients treated during the 1996–1997 period were retrieved from patient files of the Department of Urology, University Hospital »Osijek«. On screening, 28 (80%) patients with localized prostate cancer and seven (20%) patients with metastases were detected. In the group of patients examined on an outpatient basis for the signs and symptoms of prostatism, there were 30 (83.4%) patients with metastases and only six (16.6%) patients with localized prostate cancer. Study results indicated that an early diagnosis of prostate cancer could be made by use of noninvasive and inexpensive methods that cause no major discomfort to the patient. Accordingly, these results appear to strongly support such screening in men, if not in all those aged over 50, then at least in the otherwise healthy, 50–70 age group.

Key words: *prostate cancer, screening, early detection.*

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Introduction

The reasoning in favor of screening is based on the belief that radical prostatectomy or external irradiation is a life saving measure in those patients with prostate cancer who would otherwise be exposed to unavoidable tumor progression[1–5]. Such an approach appears to be logically grounded, as many patients may benefit from an early detection of the disease[7–12]. Therefore, the goal of active efforts in cancer detection is to recognize cancer at an earlier stage than it would be otherwise detected. On the other hand, there are considerable controversies and objections related to screening. Many studies against screening have appeared, especially in Europe[7]. The main objections against screening refer to its high cost, questionable impact on mortality rate, and possible unfavorable psychological effects. However, the latter does not hold, because early detection of prostate cancer is now performed by use of non-invasive methods that cause no major discomfort to the patient. The procedure consists of digital rectal examination (DRE) and determination of the prostate specific antigen (PSA) concentration[1,13].

Considering all these controversies, we embarked upon this study to point to the value of screening by determination of the percentage of localized prostate tumor (stage A and B) in patients with prostate cancer detected on screening, and in those visiting outpatient clinic for the symptoms of urination impairment or ostalgia.

Subjects and Methods

During the study, 1,000 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 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's, 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.

In the subjects in whom prostate cancer was detected, tumor clinical staging was performed by DRE, transrectal ultrasonography of prostate (TRUSP), intravenous pyelography (IVP), lung x-ray, kidney and liver ultrasonography, skeleton scintigraphy, computed tomography (CT), and marker determination, including PSA, prostate acid phosphatase (PAP), tissue specific polypeptide antigen (TPS) and bone alkaline phosphatase (BAP). Serum concentrations of total PSA were measured by PSA-RIACT radioimmunoassay (CisBiointernational, France). Data on clinical staging for prostate cancer patients treated during the 1996–1997 period were retrieved from the files of the Department of Urology, Osijek University Hospital.

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.

Percentage of localized prostate tumors

Differences in the percentage of clinically localized prostate tumor between the subjects with prostate cancer detected on screening and those in whom it was found on outpatient examination are shown in Table 2.

Thirty-five cases of prostate cancer were detected on screening. Seven (20%) of these patients had developed metastases, whereas localized prostate cancer (stage A and B) was found in 28 (80%) subjects. In the group of patients with prostate cancer detected on outpatient examination for the signs and symptoms

TABLE 1
EPIDEMIOLOGY OF PROSTATE CANCER – CLASSIFICATION OF STUDY SUBJECTS

Subjects	N	%
Healthy subjects	655	65.5
Patients		
Abnormal digital rectal examination without prostate cancer	25	2.5
Elevated PSA without prostate cancer		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 – PERCENTAGE OF LOCALIZED PROSTATE CANCER

	Stage A or B	%	Stage C or D	%	Total
Prostate cancer detected on screening	28	80.0	7	20.0	35
Prostate cancer detected on outpatient examination	6	16.6	30	83.4	36

of prostatism in the 1996–1997 period, there were 30 (83.4%) patients with metastases (stage C and D) and six (16.6%) patients with clinically localized prostate cancer. Statistical analysis of these data yielded a significant difference ($p < 0.01$)

Discussion

Early detection of prostate cancer has now been enabled by use of noninvasive methods implicating no major discomfort for the patient, such as a combination of PSA and DRE[1,13]. A carcinoma detected in its initial stage (category T_1, T_2 according to TNM classification) is likely to be limited to the prostate and potentially treatable, in contrast to a clinically manifest carcinoma[1–4].

The justification of screening for prostate cancer relies on the belief that radical prostatectomy (or external irradiation) is a life saving measure in patients who would otherwise experience unavoidable tumor progression[1–6]. This approach appears to have logical grounds, and many patients may benefit from the early detection of their disease. That is why efforts have been invested in cancer detection at an earlier stage than otherwise.

Very encouraging results were obtained at large centers, where only about 1% of tumors detected by use of PSA and DRE screening were in clinically advanced stages, which was in striking contrast with the distribution of clinically advanced cancers observed in the patient population from small centers with approximately 10%–35% of clinically advanced stage of disease[7,13–16]. It was consistent with a Swedish study, which showed 25% of patients to have developed distant metastases on initial examination. The rate was quite high, approaching the true data on about 20% of metastatic disease[15]. A study from Italy showed prostate cancer to be mostly diagnosed when the symptoms had already occurred, with local progression or dissemination of the disease in 53% of cases[15].

The results of our study differed from these reports, revealing 80% of patients with early stage disease to be detected on screening, and only 16.6% on outpatient examination of patients presenting for prostatism or other signs and symptoms of the disease. These poorer results may be attributed to the fact that patients complaining of prostatism still failed to present for urologic examination on time.

Based on the above mentioned results, those advocating screening conclude that the percentage of localized and potentially treatable prostate cancer would continue to rise with annual DRE and PSA determination, provided that selected early detection (family history) or screening of the entire male population aged ≥ 50 is performed[4,5,13–15]. The expected rise will be due to the two main reasons: 1) most advanced stage tumors will be detected and eliminated from the population; and 2) if PSA levels that were normal in the first year increase in the next year, they are more likely to rise in the range from 4.1 to 9.9 ng/ml. Accord-

ingly, the patients would be examined while the levels of PSA still remain within a low range, when the advanced disease is less likely to occur. Such a significant increase in the number of early, potentially curable lesions was demonstrated in the studies, which showed the proportion of localized prostate tumors to have increased from approximately 30% in men not included in the screening to 70%–85% in men who underwent screening with DRE and PSA[7,13–16].

Of course, it is not efficient to measure PSA levels in men younger than 50, unless their family history is burdened with cases of prostate cancer or relevant symptoms are present. The likelihood of prostate cancer rises two-fold with the existence of prostate cancer in close relatives. Neither would PSA testing be justified in men with short life expectancy due to advanced age or poor health, since such a patient would not benefit from the treatment[4,7,13–18].

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ZNAČAJ PROBIRA U OTKRIVANJU KLINIČKI LOKALIZIRANOG KARCINOMA PROSTATE

SAŽETAK

Cilj ovog rada je bio pokazati važnost probira utvrđivanjem postotka tumora ograničenih na organ (stadij A i B) u grupi bolesnika s karcinomom otkrivenim tijekom probira i u grupi onih koji su se javili u urološku ambulantu zbog simptoma vezanih uz poremećaj mokrenja ili bolove u kostima. Tijekom istraživanja pregledano je 1000 muškaraca u dobi od 50 godina i starijih, iz općine Čepin i sela Josipovac kod Osijeka. Ispitanici koji su imali povišenu koncentraciju ukupnog prostatičnog specifičnog anti-

gena i/ili suspektan digitorektalni pregled podvrgnuti su transperinealnoj biopsiji. Kod ispitanika s otkrivenim karcinomom prostate, odredili smo klinički stadij tumora, a iz arhiva klinike za urologiju, Kliničke bolnice Osijek izvadili smo podatke o kliničkom stadiju za bolesnike s karcinomom prostate liječene u razdoblju od 1996.–1997. godine. Tijekom skrininga otkriveno je 28 (80%) bolesnika s karcinomom ograničenim na prostatu i 7 (20%) s metastazama. U grupi bolesnika koji su ambulantno pregledani zbog simptoma i znakova prostatizma imali smo 30 (83.4%) bolesnika s metastazama i samo 6 (16.6%) s tumorom ograničenim na prostatu. Iz ranije navedenih rezultata proizlazi da je rana dijagnoza raka prostate moguća uporabom metoda koje nisu invazivne, nisu skupe i ne uzrokuju značajnije uznemiravanje bolesnika. Temeljem takvih rezultata može se mnogo reći u prilog probiru muškaraca, ako ne svih preko 50 godina, onda barem onih od 50 do 70 godina koji su inače dobrog zdravlja.