PROSTATE CANCER SCREENING

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Abstract
Background: Prostate cancer is a very common malignancy affecting males worldwide. There is a need to understand its risk factors, early detection and prevention approach to this disease.
Methods: Prostate cancer risk factors, early detection were reviewed from the literature and the available guidelines for screening were reviewed and summarized.
Results: Prostate cancer early detection can be done by performing digital rectal examination and obtaining prostate specific antigen (PSA). Although generally the screening is done after age 50, in some higher risk group, it should be done at younger age. However, this has to be done after discussion with the patients each individual situation. General public screening is controversial and there is no prove of impact on survival.
Conclusion: Screening for prostate cancer should be individualized and patients should be counseled about it prior to performing the test.

Prostate cancer is the most common cancer diagnosed in North American men, excluding skin cancers. It is estimated that in 2008, approximately 186,320 new cases and 28,660 prostate cancer-related deaths will occur in the United States.

Prostate cancer is now the second leading cause of cancer death in men, exceeded only by lung cancer. It accounts for 25% of all male cancers and 10% of male cancer-related deaths.(1)

Regional differences have been observed in prostate cancer incidence and mortality rates and in rates of radical prostatectomy. The increased incidence until 1989 was most likely the result of increased tumor detection due to increasing rates of transurethral prostatectomy(2, 3) Subsequent increases were most likely the result of widespread use of PSA testing for early detection and screening.(4, 5)

Risk Factors

Prostate cancer is uncommonly seen in men younger than 50 years; the incidence rises rapidly with each decade thereafter. The age-adjusted incidence is higher in African American males (258.3 per 100,000) than in white males (163.4 per 100,000)(6)

African American males have a higher mortality from prostate cancer, even after attempts to adjust for access-to-care factors.(7)

Men with a family history of prostate cancer are at an increased risk of the disease compared with men without this history.(8, 9)

Other potential risk factors besides age, race, and family history of prostate cancer include alcohol consumption, vitamin or mineral interactions, and other dietary habits.(10 – 14)

There is an association between primary tumor volume and local extent of disease, progression, and survival.(15)

A review of a large number of prostate cancers in radical prostatectomy, cystectomy, and autopsy specimens showed that capsular penetration, seminal vesicle invasion, and lymph node metastases were usually found only with tumors larger than 1.4 cc.(16) Furthermore, the

semiquantitative histopathologic grading scheme proposed by Gleason is reasonably reproducible among pathologists and correlates with the incidence of nodal metastases and with patient survival in a number of reported studies.(17)

Cancer statistics from the American Cancer Society and the National Cancer Institute indicated in 2004 that the proportion of disease diagnosed at a locoregional stage and at a distant stage is 91% and 5% for whites, compared with 89% and 7% for African Americans, respectively.(18) Stage distribution of prostate cancer is affected substantially by the intensity of early detection efforts.

With the proliferation of PSA for early detection, reviews of large numbers of asymptomatic men with prostate cancer found that most have organ-confined disease. One study found that 63% of cancers detected in men undergoing their first screening PSA were pathologically organ-confined cancers; the percentage increased to 71% if cancer was detected on a subsequent examination. (19)

Screening

Before the 1990s, the digital rectal examination (DRE) was the test traditionally used for prostate cancer screening. Two other procedures are also available: transrectal ultrasound (TRUS) imaging and serum prostate-specific antigen (PSA) concentrations.(20)

Digital Rectal Exam (DRE)

Although DRE has been used for many years, careful evaluation of this modality has yet to take place. Several observational studies have examined process measures such as sensitivity and case-survival data, but without appropriate controls and with no adjustment for lead-time and length biases.(21, 22)

Since PSA assays became widely available in the late 1980s, DRE alone is rarely discussed as a screening modality. A number of studies have found that DRE has a poor predictive value for prostate cancer if PSA is at very low levels.

In the European Study on Screening for Prostate Cancer, it was found that if DRE is used only for a PSA higher than 1.5 ng/mL (thus, no DRE is performed with PSA < 1.5 ng/mL), 29% of all biopsies would be eliminated while maintaining a 95% prostate cancer detection sensitivity. By applying DRE only for patients with a PSA higher than 2.0 ng/m, the biopsy rate would decrease by 36% while sensitivity would drop to only 92%.(23)

A previous report from this same institution found DRE to have poor performance characteristics. Among 10,523 men randomly assigned to screening, it was reported that the overall prostate cancer detection rate using PSA, DRE, and TRUS was 4.5% compared with only 2.5% if DRE alone had been used. Among men with a PSA lower than 3.0 ng/mL, the PPV of DRE was only 4% to 11%. (24)

Rectal examination is inexpensive, relatively noninvasive, and nonmorbid and can be taught to nonprofessional health workers; however, its effectiveness depends on the skill and experience of the examiner. The possible contribution of routine annual screening by rectal examination to reducing prostate cancer mortality remains to be determined.

Transrectal Ultrasound and Other Imaging Tests

Imaging procedures have been suggested as possible screening modalities for prostate cancer. Prostatic imaging is possible by ultrasound, computed tomography, and magnetic resonance imaging. Each modality has relative merits and disadvantages for distinguishing different features of prostate cancer. Ultrasound has received the most attention, having been examined by several investigators in observational settings.(25)

Sensitivity ranged from 71% to 92% for prostatic carcinoma and 60% to 85% for subclinical disease. Specificity values ranged from 49% to 79%, and positive predictive values in the 30% range have been reported. The sensitivity and positive predictive value for ultrasound as a single test may be better than for rectal examination. The rate of cancer is extremely low among ultrasound-positive patients in whom rectal and PSA examinations are normal.(26)

Contemporary prostate biopsy relies on spring-loaded biopsy devices that are either digitally guided or guided via ultrasound. TRUS guidance is the most frequently used method of directing prostate needle biopsy because there is some suggestion that the yield of biopsy is improved with such guidance.(27)

With the virtually simultaneous clinical acceptance of TRUS, spring-loaded biopsy devices, and the proliferation of PSA screening in the late 1980s, the number of prostate cores obtained from patients with either an abnormal DRE or PSA was most commonly six, using a sextant method of sampling the prostate.(28)

There is evidence that the predictable increase in cancer detection rates that would be expected by increasing the number of biopsy cores beyond six does occur; e.g., biopsies with 12 or 15 cores would increase the proportion of biopsied men having cancer detected by 30% to 35%.(29, 30)

The extent to which such increased detection will reduce morbidity and mortality from the disease or increase the fraction of men treated unnecessarily is unknown.

Prostate-Specific Antigen (PSA)

The PSA test has been examined in several observational settings for initial diagnosis of disease, as a tool to monitor for recurrence after initial therapy, and for prognosis of outcomes after therapy. There is no PSA value below which a man can be assured that he has no risk of prostate cancer. Parameter estimates for this test include sensitivity in the range of 70%.(31)

The potential value of the test appears to be in its simplicity, objectivity, reproducibility, relative lack of invasiveness, and relatively low cost. PSA has increased the detection rate of early-stage cancers, many of which may be curable by local-modality therapies.(32-35)

Experience with repeat PSA screening suggests that tumors detected on follow-up examinations are of lower clinical stage and grade.(36)

Although a cutoff value of 4.0 ng/mL is frequently used to prompt prostate biopsy, screening studies have demonstrated that lowering the PSA cutoff will substantially increase the number of cancers detected, particularly in African Americans.(37)

An initial PSA lower than 2.5 ng/mL is associated with a very low risk of cancer detection within a 4-year follow-up.(36-38)

The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) is a multicenter, randomized, two-armed trial designed to evaluate the effect of screening for prostate, lung, colorectal, and ovarian cancer on disease-specific mortality. Enrollment began in November 1993 and concluded in June 2001. Participants were randomly assigned to the screening or control arm. A total of 76,705 men were enrolled, 38,250 of whom were assigned to the screening arm. Of these, 34,244 men underwent an initial PSA and/or DRE screening examination. Compliance rates for PSA and DRE were roughly equivalent at 89%. More than 99% of men who underwent screening with either PSA or DRE received both screening tests.(39)

Table 1: Summary of Prostate, Lung, Colon and Ovarian (PLCO) Screening

Screening Test Administered	PSA N0 (%)	DRE N0 (%)	PSA or DRE N0 (%)
Number of Men Receiving Test	34, 233	34, 115	34, 224
Positive Test (%): DRE Suspicious for Cancer; PSA >4 ng/mL	2, 717 (7.9)	2, 482 (7.3)	4, 801 (14.1)
Biopsies (% of positives)	1, 112 (40.9)	639 (25.7)	1, 510 (31.5)
Prostate Cancer (% of biopsies)	489 (44.0)	219 (34.3)	556 (36.8)
Prostate Cancer (% of positives)	489 (18.0)	219 (8.8)	556 (11.6)

PSA: Prostate specific Antigen. DRE: Digital Rectal Examination

Various approaches aimed at improving the performance of PSA in early cancer detection have been tested. None are clearly more accurate than total serum PSA levels, but these approaches are listed below.

- Complexed PSA and percent-free PSA
- Third-generation PSA
- PSA density
- PSA density of the transition zone
- Age-adjusted PSA
- PSA velocity

Frequency of screening

The optimal frequency and age range for PSA (and DRE) testing are unknown (40, 41). Cancer detection rates have been reported to be similar for intervals of 1 to 4 years. (42)

Table 2: American Cancer Society Recommendation

Population	Age	Performing PSA, DRE
Average risk	≥ 50	Only after discussing risk-benefits and patient agrees
Moderate high risk (one first degree relative with prostate cancer <65)	≥ 45	
High risk (several first degree relatives with prostate cancer)	≥ 40	

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