American Cancer Society Guideline for the Early Detection of Prostate Cancer: Update 1997

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In 1997, based on revised projections, prostate cancer will be diagnosed in an estimated 209,900 American men; 41,800 will die of the disease, making it the second leading cause of cancer death in men after lung cancer.[1] Prostate cancer accounts for 36% of all male cancers in the United States and 13% of cancer-related deaths in men.

The incidence of prostate cancer is 66% higher among African-American men than among white men. In fact, African-American men experience the highest prostate cancer incidence rates in the world, and associated mortality rates are twice those of white men. Nineteen percent of all cancer deaths among African-American men are caused by prostate cancer.[2]

The disease is common in North America and northwestern Europe and is rare in the Near East, Africa, and South America. The familial tendency to develop prostate cancer may be the result of genetic or environmental factors. Some research suggests that dietary fat may also play a role in the development of prostate cancer.[2]

Between 1988 and 1992, the incidence of prostate cancer in the United States increased dramatically. This increase has been attributed largely to the introduction and widespread application of prostate-specific antigen (PSA) screening. During the same period, a shift occurred to an earlier stage at the time of diagnosis; that is, the number of cases of local and regional disease at diagnosis increased, and the finding of distant disease at diagnosis decreased. Overall 5-year prostate cancer survival rates also increased.

No direct evidence exists to date to show that PSA screening decreases prostate cancer mortality rates. Prospective studies are underway to examine this potential link, but so far none has documented any reduction in mortality as a direct result of screening. Indirect evidence, however, suggests that prostate cancer

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screening has resulted in the diagnosis of earlier-stage disease in more younger men, which could influence mortality.

Update of Guideline

In 1992, the American Cancer Society issued the following prostate cancer screening recommendation: Men age 50 years and older should undergo digital rectal examination and PSA testing annually. If either is abnormal, further evaluation should be considered.

In March 1997, the ACS convened a workshop to review this guideline in light of the expanding body of clinical research data about prostate cancer screening and early detection. Based on compelling intermediate data from ongoing clinical tri-

should begin at age 50 years. However, men in high-risk groups, such as those with a strong familial predisposition (e.g., two or more affected first-degree relatives), or African-Americans may begin at a younger age (e.g., 45 years). More data on the precise age to start prostate cancer screening are needed for men at high risk.

• Screening for prostate cancer in asymptomatic men can detect tumors at a more favorable stage (disease confined to the prostate). Mortality from prostate cancer has decreased, but it has not been established that this event has resulted directly from screening.

• An abnormal PSA test result has been defined as a value of more than 4.0 ng/ml. Some elevations in PSA may be caused

The updated ACS prostate cancer screening guidelines are based on compelling intermediate data from ongoing clinical trials.

als suggesting that prostate cancer screening may result in the discovery of more early-stage disease (and therefore a potential increase in the cure rate), the ACS updated the 1992 guideline. The Board of Directors of the ACS approved the following updated guideline on June 10, 1997: The ACS recommends that both the PSA test and the digital rectal examination be offered annually, beginning at age 50, to men who have a life expectancy of at least 10 years and to younger men who are at high risk. Information should be provided to patients about the risks and benefits of screening.

Narrative

The narrative accompanying the guideline provides the following additional information:

• Men who choose to undergo screening

by benign conditions of the prostate.

• Digital rectal examination of the prostate should be performed by health care professionals skilled in recognizing subtle prostate abnormalities, including those of symmetry and consistency, as well as the more classic finding of marked induration or nodules. Digital rectal examination is less effective in detecting prostate cancer than is PSA testing.

The updated guideline emphasizes the need to give patients more information about the risks and benefits of intervention and offers further guidance for men at high risk or advanced age. For instance, the ACS now recommends that physicians inform prostate cancer patients that a PSA value less than 4.0 ng/ml does not guarantee that cancer is not present, because up to 25% of men with the disease can have PSA levels less than 4.0 ng/ml. Furthermore, an "abnormal" or el-

evated PSA level can result from benign growth, inflammation, or other causes. Therefore, many men with elevated PSA levels may require additional diagnostic tests and in the end may not require treatment. Information such as this will help patients faced with decisions about screening and any subsequent treatment.

Controversy surrounds prostate cancer screening because of the complexity and variability of the disease process, the slow-growing nature of many malignancies, and the limited accuracy of screening tests. Although PSA testing is strongly associated with the increased incidence of prostate cancer noted in recent years, some cancers detected by PSA level may be latent or indolent and thus unlikely to produce clinical symptoms or affect survival.

benign prostatic hypertrophy and no malignancy have an elevated PSA level.

Widespread screening for prostate cancer may result in the detection of many malignancies with unpredictable future effects on morbidity and mortality. Some study data, however, suggest that cancers detected by PSA screening may be more important clinically than are latent cancers. Because no methods are available to distinguish between slow-growing cancers and more clinically significant early-stage cancers, clinicians are faced with the difficult decision of whether to prescribe watchful waiting without clinical intervention or to pursue aggressive therapy.

Men whose screening results are positive are faced with the difficult decision of whether to submit to curative

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Some abnormal PSA levels (more than 4.0 ng/ml) may be caused by benign conditions of the prostate.

It is also likely that some men with prostate cancer, especially older men, may die of other causes before the cancer presents itself clinically. Autopsy studies have shown that prostate cancer, microscopic or otherwise, may be present in 33% of men over the age of 50 years.[3] When these findings are considered in aggregate with United States census data, the results suggest that millions of American men have prostate cancer in some form.[4]

The accuracy of the PSA test is also central to discussions about prostate cancer screening. PSA values of more than 4.0 ng/ml are generally considered abnormal. Sensitivities as high as 80% and as low as 29% have been reported for the PSA test based on this cutoff point. In addition, conditions such as benign prostatic hypertrophy and acute bacterial prostatitis may produce a high number of false-positive results. About 25% of men with

therapy, such as radical prostatectomy or radiation treatment, and the accompanying risks, which include incontinence, impotency, and other complications. The rising incidence of prostate cancer that has resulted from more ambitious screening efforts has already led to an increase in the number of radical prostatectomies and radiation treatments performed in the United States.

Critical Research Issues

Much has been learned in recent years about the techniques and impact of early prostate cancer detection. Many critical research questions, however, remain to be addressed, including the following:

The influence of known prostate cancer risk factors on the optimal age at which screening should be initiated. Of particular interest is the age at which screening of men with a family history or the pres-

ence of genetic risk is justifiable and cost-effective. The same uncertainty pertains to the precise age at which African-Americans may begin to benefit from screening.

The influence of patient characteristics, risk factors, and previous test outcomes on the optimal screening interval. Whether the screening interval may be lengthened in men with low initial PSA levels or repeated normal examinations deserves investigation. A similar inquiry could be directed to the possible need for a shorter screening interval in men with associated risk factors.

The psychosocial impact of screening. The reassurance gained from a false-negative test and the anxiety produced by a false-positive test are worthwhile topics for behavioral research.

Cost-effectiveness. Different strategies for the efficient delivery of screening (e.g., cost productivity, missed diagnosis, cost of dying from prostate carcinoma) should be studied to yield the most cost-effective medical care.

Enhancements of PSA testing. Several different measures of PSA—including density, velocity, doubling time, form (free versus complexed), and age-specific and race-specific PSA—have been proposed as enhancements to the testing of PSA level. No superiority of any single alternative strategy has been shown, but further research is warranted.

New tests. Tests that may complement or serve as alternatives to PSA and tests that may predict the aggressiveness of disease require rigorous evaluation. Among these new tests are prostate-specific membrane antigen, telomerase, and prostate markers in other body fluids (such as seminal fluid, urine, saliva).

Imaging techniques. Imaging enhancers may improve the accuracy of guided biopsy techniques such as ultrasound.

Biopsy technique. Research should be conducted to determine the optimal biopsy procedure with respect to factors such as the number of cores and the site of biopsy (e.g., prostate transitional zone versus peripheral zone).

Follow-up of negative biopsy. The optimal follow-up interval should be assessed.

Need for more trials. More population-based and case-controlled studies are needed to assess the efficacy of current screening practices.

Impact of early detection. Data showing decreased mortality, earlier stage at diagnosis, and decrease in associated comorbidities need to be modeled to project better the long-term effect of screening on the United States population.

Definition of high-risk groups. More studies are needed (such as those based on diet, race, family history, and other unknown factors) to define high-risk groups.

Summary

In summary, the 1997 revision of the ACS guideline for the early detection of prostate cancer is based on knowledge gained by a critical analysis of experience since the original version of 1992. This is only a milestone along a continuous journey rather than being the final destination. Other revisions will be considered when new knowledge becomes available, but for the present, this guideline is offered to health care professionals seeking to provide optimal care to asymptomatic men at risk for prostate cancer. CA

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