

Update on Prostate Cancer Screening Guidelines

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Abstract and Introduction

Introduction

In the United States, prostate cancer is the most common type of cancer in men irrespective of race or ethnicity. ^[1] Earlier detection of prostate cancer through the prostate-specific antigen (PSA) test resulted in an upswing in cases from the mid-1980s to the mid-1990s. ^[2]

Until recently, the PSA test was the gold standard as part of physical examinations for men, especially in those older than 50 years of age. As of October 2011, however, the U.S. Preventive Services Task Force (USPSTF) no longer recommends that men older than 50 years routinely receive PSA testing.^[3] This is because there is no consensus that screening for prostate cancer saves lives, and also because treatment often leads to complications (e.g., impotence and incontinence). As a result, the decision to undergo prostate cancer screening now involves weighing the potential risks and benefits of screening. An active-surveillance approach to deciding when and if treatment is appropriate may also be considered if the cancer is found to be progressing. However, there are lifestyle modifications, such as engaging in vigorous physical activity, that may reduce the risk of advanced prostate cancer.

Background

According to the American Cancer Society (ACS), about 1 in 6 men will be diagnosed with prostate cancer during the course of a lifetime, and about 1 in 36 will die of the disease. ^[4] Most prostate cancers grow slowly, but in some cases progression is quick. In several studies, autopsies of older men who died from other diseases revealed that many of the patients also had undiagnosed prostate cancer. ^[5] According to these studies, as many as 7 to 9 out of 10 patients had prostate cancer by 80 years of age. ^[5] Scientists believe that prostate cancer begins with prostatic intraepithelial neoplasia (PIN)—microscopic changes in the size and shape of prostate cells.

Risk Factors and Warning Signs

It is important to identify men with significant risk factors for prostate cancer. Risk factors include age, race/ethnicity, family history, and classification of PIN. Age is one of the strongest risk factors, with a rapid increase in risk after age 50 years. ^[6] Prostate cancer occurs more commonly in African American men and in men living in North America, northwestern Europe, Australia, and the Caribbean Islands. ^[6] The risk is almost doubled if a man has a brother or father with prostate cancer, suggesting that there is a genetic component. ^[6] The risk of prostate cancer is higher if a biopsy reveals high-grade (abnormal) PIN. ^[2] Some of the warning signs of prostate cancer include difficulty urinating, a weak or interrupted urine flow, erectile dysfunction, pain or discomfort in the pelvic area, and bone pain. ^[7]

Screening

Traditionally, prostate cancer screening was recommended to detect the disease at earlier, asymptomatic stages, when treatment might be more effective. ^[3] Two tests are used to screen for prostate cancer. The first test is the digital rectal examination (DRE), in which the physician checks for lumps in the prostate by inserting a lubricated, gloved finger into the rectum. Tumors often grow in the area of the prostate next to the rectum. ^[8] The presence of a hard or even spot may signal prostate cancer. The second form of evaluation is a blood test used to detect the amount of PSA protein circulating in the blood. In general, the higher a patient's PSA level, the greater the chance that cancer is present. ^[9] Alone or in combination, these tests cannot confer a definitive diagnosis of prostate cancer; in every case, a prostate biopsy is required to make the diagnosis. Other causes of elevated PSA include benign prostatic hyperplasia (BPH), prostatitis, and recent prostate biopsy or DRE. ^[10] It is important to be aware that PSA levels are low in some early-stage prostate cancers. ^[11]

The USPSTF's Review of Evidence

The USPSTF last reviewed the evidence on prostate cancer screening and made recommendations in 2008. In an effort to update these guidelines, the USPSTF conducted an exhaustive review of randomized trials of PSA-based screening, randomized trials and cohort studies of prostatectomy or radiation therapy versus watchful waiting (using changes in symptoms to decide whether treatment is needed), and large observational studies of perioperative harms. ^[3,12] This review sought to answer four key questions: (1) Does PSA-based screening decrease prostate cancer– specific or all-cause mortality? (2) What are the harms of PSA-based screening-detected prostate cancer? (3) What are the benefits of treatment of early-stage or screening detected prostate cancer? See , , , and for a summary of the evidence. ^[13]

Studies (n) and Overall Quality	Summary of Findings
5 RCTs Overall quality: fair	PSA-based screening identifies more prostate cancers, but most trials found no effect on risk of death from prostate cancer. The 2 largest, highest-quality trials reported conflicting results: In ERSPC, PSA screening every 2–7 y was associated with decreased risk of death from prostate cancer in a subgroup of men aged 55–69 y after 9 y, but PLCO found no effect after 10 y. In 3 poor-quality screening trials, there was no association between PSA-based screening and decreased risk of death from prostate cancer.

 Table 1. Does PSA-Based Screening Decrease Prostate Cancer–Specific or All-Cause Mortality?

ERSPC: European Randomized Study of Screening for Prostate Cancer; PLCO: Prostate, Lung, Colorectal, and Ovarian Cancer screening trial; PSA: prostate-specific antigen; RCT: randomized, controlled trial. Source: Reference 13.

Studies (n) and Overall Quality	Summary of Findings	
2 RCTs	Both trials had false-positive rates of 12%-13% after 3–4 rounds of PSA-based screening, and 1 trial found that 76% of prostate biopsies identified no cancer.	

Table 2. What Are the Harms of PSA-Based Screening for Prostate Cancer?

Overall quality: Serious infections or urine retention occurred after 0.5%-1.0% of prostate biopsies. fair

PSA: prostate-specific antigen; RCT: randomized, controlled trial.

Source: Reference 13.

Table 3. What Are the Benefits of Treatment of Early-Stage or Screening-Detected Prostate Cancer?

Studies (n) and Overall Quality	Summary of Findings
Prostatectomy: 2 RCTs, 8 cohort studies Overall quality: fair	Prostatectomy was associated with decreased risk of prostate cancer–specific mortality and all-cause mortality vs. watchful waiting after 15 y of follow-up in 1 good-quality RCT. Subgroup analysis suggests that benefits are limited to men <65 y. In observational studies, prostatectomy was associated with decreased risk of death from prostate cancer (6 studies) and all-cause mortality (5 studies) after 4–13 y of follow-up vs. watchful waiting.
RT: 5 cohort studies Overall quality: fair	RT was associated with decreased risk of prostate cancer–specific mortality (5 studies) and all-cause mortality (5 studies) after 4–13 y of follow-up vs. watchful waiting.

RCT: randomized, controlled trial; RT: radiation therapy.

Source: Reference 13.

Table 4. What Are the Harms of Treatment of Early-Stage or Screening-Detected Prostate Cancer?

Studies (n) and Overall Quality	Summary of Findings
Prostatectomy: 18 studies—1 RCT, 11 cohort studies, 6 uncontrolled observational studies Overall quality: fair	Prostatectomy was associated with increased risk of UI vs. watchful waiting in 1 RCT and 4 cohort studies. Based on large databases and surgical series, prostatectomy was associated with risk of perioperative death (~0.5%) and CVEs (0.6%-3%).
RT: 14 studies—1 RCT, 13 cohort studies Overall quality: fair	RT was associated with increased risk of ED vs. watchful waiting in 6 cohort studies. Risk of UI was increased in 1 RCT with a highly imprecise estimate, but not in 4 cohort studies. RT was associated with increased risk of bowel dysfunction that appeared to improve over time.

CVE: cardiovascular event; ED: erectile dysfunction; RCT: randomized, controlled trial; RT: radiation therapy; UI: urinary incontinence.

Source: Reference 13.

The USPSTF concluded that the PSA test was more likely to lead to a substantial risk than to a benefit. The PSA test cannot differentiate between aggressive and nonaggressive cancers, which may result in many men undergoing needless surgery and radiation that expose them to significant side effects. According to the USP-STF, up to 5 men in 1,000 will die within a month of prostate cancer surgery, and approximately 10 to 70 men will experience dangerous complications. ^[3] At least 200 of every 1,000 men treated with radiation or surgery will experience impotence, urinary incontinence, or bowel dysfunction. ^[3] The USPSTF considers these to be serious risks, considering that its review found that PSA screening has not been proven to save lives.

Other Opinions

The USPSTF has determined that PSA-based screening is associated with detection of more prostate cancers, results in little reduction in prostate cancer mortality, and may lead to harms (related to false-positive test results and subsequent treatment). ^[3] The largest clinical studies the USPSTF has examined so far have not found a statistically significant reduction in deaths from prostate cancer among men who had the PSA test compared with those who did not. Not all experts agree with the USP-STF's recommendations, however; many support an approach of active surveillance. This involves closely monitoring for cancer via screening tests at regular intervals and then considering treatment options if test results indicate cancer progression. ^[12]

Shortly after the USPSTF released its report, the American Urological Association (AUA) issued a statement in response. The AUA's stance is that an appropriately interpreted PSA test provides important information concerning the diagnosis, pretreatment staging or risk assessment, and monitoring of prostate cancer patients. ^[14] The AUA recommends that once a diagnosis of prostate cancer is made, the patient should discuss with his urologist whether active surveillance or treatment is appropriate. ^[14] This is because not all prostate cancers require treatment, and not all are life-threatening. ^[14]

The ACS also recommends that a patient consult his physician, consider the risks and benefits, and make an informed decision about whether to be screened for prostate cancer. ^[15]

Lifestyle Modifications

Even if a patient decides against being screened for prostate cancer, there are lifestyle modifications that can help reduce the risk of advanced or lethal disease. Most older men have prostate cancer, but the type of prostate cancer is what is significant. ^[2] The most promising lifestyle modification to lower the risk of advanced disease is to increase the amount of physical activity. A 2005 study found that older men who engaged in vigorous activities such as jogging, biking, swimming, or tennis had a 70% lower risk of advanced or lethal cancer. ^[16] Even though staying lean does not cut the risk of being diagnosed with prostate cancer, it may decrease mortality. ^[17] A healthy body weight at or before diagnosis is a strong predictor of survival. ^[2] Additionally, the benefits of exercising and losing weight go beyond decreasing the risk of prostate cancer. Studies examining the effect of taking vitamin E, selenium, lycopene, vitamin D, or calcium have conflicting results; therefore, no definitive conclusion concerning the effect of these lifestyle modifications can yet be made. ^[16–22]

Conclusion

Because it detects prostate cancer earlier, the PSA test has been routinely performed as part of a man's physical examination. Based on a comprehensive review of evidence, the USPSTF has concerns about PSA testing and no longer recommends routine screening; however, the AUA and other experts disagree. Patients should discuss the risks and benefits of PSA screening with their physician and make an informed decision.

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