Prostate Cancer Screening

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KEYWORDS

• Prostate-specific antigen testing • PSA screening • Shared decision-making
• Elevated PSA

KEY POINTS

- A clinician and patient should engage in shared decision-making before engaging in prostate-specific antigen (PSA) testing.
- The PSA test is the most common method to determine a man's risk of having prostate cancer, but it is not cancer specific.
- There are additional tests beyond the PSA test to stratify a man's risk of having prostate cancer.

OVERVIEW

Prostate cancer is the most common nonskin cancer in men in the United States with approximately 1 in 7 men developing prostate cancer, and it is the third leading cause of cancer death in men.[1] In 1994, the US Food and Drug Administration (FDA) approved the use of prostate-specific antigen (PSA) screening to test asymptomatic men for prostate cancer and, since implementation, the incidence of metastasis and mortality from prostate cancer have significantly decreased.[2,3] However, the use of PSA screening for prostate cancer has its limitations. Although it is very prostate-specific it is not cancer-specific. Other factors besides prostate cancer, such as an enlarged prostate or prostatitis, can cause an elevated PSA. In addition, PSA levels serve as a continuum in which the risk of prostate cancer increases with increasing PSA, but there is no level of PSA below which the risk of prostate cancer can be eliminated. Even though prostate cancer is very common, a man only has a 2.6% risk of dying from it because most cases of prostate cancer are slow growing and may never cause morbidity or mortality.[4]

CONTROVERSIES OF PROSTATE-SPECIFIC ANTIGEN TESTING

There is criticism that prostate cancer is overdiagnosed and overtreated in the United States. Numerous studies have been conducted to try to quantify the mortality benefits of PSA screening. Although it is known that PSA testing leads to a higher incidence

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of cancer detection, it is unknown whether the increased detection is accompanied by a significant reduction in mortality that also outweighs the harms of overdetection and overtreatment. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Study of Screening for Prostate Cancer (ERSPC) are the most commonly referenced studies in the literature regarding this issue. Although the PLCO trial demonstrated no benefit from PSA screening, the trial had flaws, such as a high contamination rate, and a reanalysis published in the *New England Journal of Medicine* in 2016 confirmed that.[5] The ERSPC trial demonstrated a significant prostate cancer mortality benefit with PSA screening, but it is unknown whether the benefit outweighed the harms of screening that can lead to the overdiagnosis and overtreatment of prostate cancer. These were the 2 main studies the US Preventive Services Task Force (USPSTF) used when they gave a grade D recommendation against screening for prostate cancer in May 2012, which caused a great deal of controversy.[6] However, the USPSTF revised their recommendation in 2017 giving PSA screening a grade C for men ages 55 to 69 years and maintained their grade D recommendation for men ages 70 years and older.[7]

GUIDELINES

Two organizations, the American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN), have guidelines to help clinicians use PSA testing (**Table 1**). Shared decision-making with the patient is a concept that holds true throughout all prostate cancer detection guidelines. A patient must know the risks, benefits, and alternatives of prostate cancer screening before making an informed decision. Even though the AUA and NCCN have put forth guidelines for clinicians it must be remembered that guidelines are no substitute for clinical judgment or experience. With all the confusion surrounding PSA testing, it can be difficult to determine the best course of action for a patient. However, an excellent place to start is to recognize the inherent strengths and weaknesses of the USPSTF recommendations. Second, it is important to engage in shared decision-making with the patient. Third, identify the patients who will likely benefit the most from screening based on risk factors, such as age 55 to 69 years, African American race, and family history of prostate cancer. Fourth, consider a baseline PSA test between the ages of 45 to 54 years. A higher PSA in midlife is associated with a higher risk of future prostate cancer and this baseline value can help stratify a patient's risk to better determine frequency of testing.[8,9] Finally, refer to a health care provider who specializes in urology when faced with a confirmed elevated PSA, an abnormally rising PSA, an abnormal digital rectal examination (DRE), or a patient with significant risk factors. There are new and emerging tests available to better stratify a patient's risk of having or dying from prostate cancer, such as biomarkers, genomic testing, and multiparametric MRI. Collaboration between the patient, clinicians in primary care, and urology is paramount to optimize patient outcomes.

MANAGING AN ELEVATED PROSTATE-SPECIFIC ANTIGEN

The half-life of PSA is approximately 3 days, so when encountering an abnormal PSA test it is prudent to repeat the test 1 month later for confirmation.[10,11] One study demonstrated that approximately 25% of men with an initial PSA between 4 and 10 ng/mL had normal PSA levels on repeat testing.[12] Also, when facing an elevated PSA in an asymptomatic man, the AUA, as part of the Choosing Wisely campaign, recommends against prescribing a course of antibiotics before rechecking a PSA value because there is a lack of clinical studies to show that antibiotics actually decrease PSA levels in