Personalizing Prostate-Specific Antigen Screening Intervals for Prostate Cancer Detection

Aus G, Damber JE, Khatami A, et al. Individualized screening interval for prostate cancer based on prostate-specific antigen level: results of a prospective, randomized, population-based study. Arch Intern Med 2005;165:1857–61.

Study Overview

Objective. To evaluate the relationship between serum prostate-specific antigen (PSA) levels and cumulative risk of prostate cancer and to determine if PSA testing intervals can be individualized based on PSA level.

Design. Secondary analysis of a prospective, randomized, population-based study.

Setting and participants. In Göteborg, Sweden, 20,000 men were randomized to either a control or an intervention group, which included regular PSA testing. For the purposes of this study, only individuals randomized to PSA screening were included in this analysis (n = 5855).

Main outcome measures. The primary outcome was a new diagnosis of prostate cancer. Men with PSA levels ≥ 3.00 ng/mL were referred for further workup, including transrectal ultrasonography and laterally directed sextant biopsies. Men with benign biopsy results but with PSA levels ≥ 7.00 ng/mL underwent 6-month follow-up PSA testing and repeat biopsy if indicated. Projected cumulative risk of prostate cancer were estimated with Kaplan-Meier curves.

Main results. 5855 men were included in the analysis (mean age, 57.9 years; median follow-up, 7.6 years), 539 of whom (9.2%) were diagnosed with prostate cancer. On initial PSA testing, 661 men had levels ≥ 3.00 ng/mL and were offered biopsies. No men with PSA levels < 0.50 ng/mL were diagnosed with prostate cancer during the study period. After 3 years, the cumulative detection rate was 0% for the 2950 men with PSA levels < 1.00 ng/mL, 0.07% for the 4088 men with baseline PSA levels < 1.50 ng/mL, and from 12.3% to 25.2% for the 1106 men with baseline PSA levels from 1.50 to 2.99 ng/mL.

Conclusion. Re-testing intervals for PSA could be individualized based on PSA levels. Men with PSA levels < 1 ng/mL could be safely followed with 3-year testing intervals.

Commentary

Prostate cancer is one of the most common cancers in men in Western cultures and is associated with significant morbidity and mortality, with an estimated 30,000 deaths expected for 2005 in the United States [1]. The ideal means to screen for prostate cancer has yet to be determined [2]. Currently, most organizations advocate PSA testing (in annual or biannual testing intervals) but only after a thorough discussion of its potential risks and benefits with the patient [3,4]. Unlike colorectal cancer, for which screening intervals are based on a well-understood timeline for tumor progression, screening intervals for prostate cancer are relatively arbitrary.

Prior epidemiologic data have consistently demonstrated a positive correlation between PSA level and prostate cancer risk [5,6]. Aus et al have contributed to this literature by determining the cumulative risks of prostate cancer associated with varying baseline PSA levels. The investigators found that in men with baseline PSA levels less than 1 ng/mL, the cumulative detection rate of prostate cancer over a 3-year period was 0%. In addition, cumulative risks for detecting prostate cancer were surprisingly high in patients with baseline PSA levels over 1.50 ng/mL. Cumulative risks varied from 12.3% in individuals with baseline levels of 1.50 to 1.99 ng/mL to 33.3% for men with PSA levels of 3.00 to 3.99 ng/mL.

One potential limitation of the study was the PSA level that the investigators specified as requiring referral for a biopsy (ie, ≥ 3.00 ng/mL). Recent evidence has demonstrated that occult prostate cancer can be detected from biopsy specimens in men with PSA levels less than 3.00 ng/mL [7]. Thus, cases of prostate cancer associated with low levels of PSA might have been missed. It is still unclear whether these microscopic foci need to be identified and removed as early as possible or whether they could be followed until the PSA level begins to rise. Because the incidence of prostate cancer microfoci far exceeds the number of fatalities related to the disease, it is generally believed that watchful waiting is an acceptable strategy.

Applications for Clinical Practice

Aus et al's findings support other data suggesting that men

with low baseline PSA levels (< 1.00 ng/mL) are unlikely to benefit from annual or even biannual PSA testing. Men with higher PSA levels (≥ 1.50 ng/mL) have a substantially higher risk of prostate cancer and should be followed with annual testing.

–Review by Harvey J. Murff, MD, MPH

References

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