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RESEARCH HIGHLIGHT

Prostate-specific antigen (PSA) screening: has the pendulum swung too far?

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Prostate-specific antigen (PSA) along with digital rectal exam has been the standard for prostate cancer screening in the United States for the past 20 years.[1] During this time period, the improved detection of prostate cancer decreased related mortality more than 30%.[2] In fact, metastases and their comorbidities have decreased more than 75% since the early 1990s, resulting in a higher incidence of early organ-confined disease. While it is clear that prostate cancer mortality statistics have improved, it is unclear whether men are overscreened.

To better understand who should be tested, the American Urological Association and American Cancer Society published guidelines recommending PSA screening be offered to men with a 10-year or greater life expectancy.[3] In addition, initiation of screening should begin at age 40–50 years depending on risk factors. Since younger individuals benefit the most from screening, the PSA threshold to screen these men is age-adjusted.

The guidelines to stop or temporarily hold screening are mixed. The American Urological Association and American Cancer Society recommend basing the decision only on the 10-year life expectancy due to age and morbidity. The United State Preventative Task Force, meanwhile, suggests an age-based cutoff at 75 years of age.

Once a patient's PSA laboratory value is abnormal, he will most likely receive a prostate biopsy for diagnosis. Given the fact that less than 10% of Americans select active surveillance, screening starts a snowball effect that usually 'buys' a treatment. However, many individuals diagnosed with prostate cancer will not be directly affected by its effects. They will pass away from another cause and the knowledge of prostate cancer will not have benefited them. Instead, the knowledge of prostate cancer may cause emotional, financial and physical harm.[4,5] The critical questions, then, revolve around when and whom to screen.

Drazer and colleagues recently performed a cross-sectional analysis of over 14 000 men whose data were extracted from the United States National Health Interview Survey to better understand PSA screening trends.[6] As expected, PSA screening rates varied by age, demonstrating bell shape distribution peaking at 47% for men in their seventies and trailing off for the young and very old. Notably, however, 25% of men over the age of 85 years continued to be screened for their PSA independent of their health status. This fact alone brings rise to the question of the need for institutional PSA ordering guidelines. Interestingly, the most screened age was men in their seventies even though younger patients have a greater potential to benefit from a >10-year life expectancy.

The authors then stratified the men over 70 years into life expectancy groups using 5 years as the cutoff: high (<15% mortality), intermediate (16%–47% mortality) and low (>48% mortality). As expected, populations adjusted for age with a higher life expectancy had higher screening rates: 47%, 39% and 30% for high, intermediate and low life expectancy rates, respectively. This trend continued across all ages. Strikingly, however, individuals with low life expectancies continued to be screened roughly 30% of the time, peaking at 45% for men of 75–79 years old even though these men had a 50:50 chance of dying in the next 5 years from non-prostate-related causes.

From Drazer's study, factors independently associated with increased screening rates were age and life expectancy. Other factors corresponding with increased screening included higher education, access, marriage and consistency with other healthcare recommendations (colorectal cancer screening, limited alcohol intake, non-smoking and yearly doctor's visit). These findings make sense. Individuals who have better access, who are responsible, or who are healthier, would be expected to seek screening. Interestingly, comorbidities such as chronic obstructive pulmonary disease, diabetes, cancer history and obesity did not correlate with changes in screening. However, needing help with daily activities and older age correlated with decreased PSA screening levels.

Drawing conclusions from Drazer's study, the authors note that patients in the low life expectancy groups and the older age groups are overscreened for prostate cancer. Other studies have also demonstrated the discrepancy between screening in theory and in practice. The Veteran's Administration evaluated PSA screening with both age and life expectancy and found that health did not impact screening rates.[7] In fact, 85-year-old men in either good or bad health were both screened roughly one-third of the time supporting the findings in the Drazer study.

The impetus behind continued screening is unclear. Studies have cited fear of legal backlash, belief that any screening is beneficial, and patient desire. Physicians may also not understand or take the time to evaluate life expectancy. In addition, patients may not understand the ramifications of pan-screening. However, the cost/benefit ratio is much higher for those who are not proper candidates for screening.[8] In Drazer's study, over 21% of patients who were both >85 years and had a 50% 5-year survival were still screened. Are these individuals benefiting from prostate cancer screening? Possibly they are deriving satisfaction from knowledge, but not treatment. The costs can be high.

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Despite the notion that men are being overscreened for prostate cancer, the importance of screening cannot be underestimated. Studies such as the Göteborg trial have demonstrated that screening will reduce prostate cancer mortality.[9] Specifically, 293 men needed to be invited for screening and 12 to be diagnosed to prevent one prostate cancer death. This study population, however, included individuals under 71 years of age, which once again highlights the discrepancy between elderly or frail individuals who will not benefit from screening.

If the goal is to improve the selection of individuals who would benefit from prostate cancer screening, then a hard look needs to be taken at screening practices. There is currently a diminishing return proportional to age and 10-year mortality. If one is looking for the tools, the Charlson index is currently the strongest predictor of non-cancer-specific mortality.[10] More precise biomarkers are needed to differentiate aggressive versus indolent cancers. In the future, genetic testing, improved biomarkers, prevention and life expectancy changes will shift the screening guidelines, further defining the pool of appropriate individuals to screen. But the question will still remain the same: will diagnosing prostate cancer improve this patient's life?

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