Opinion
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Should (healthy) elderly males be spared a prostate-specific antigen (PSA) screening test

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Opinion

Defining "elderly" can vary by age group but is often considered to start at the age 65. The percentage of elderly people varies significantly and is projected to grow in the coming years. A "young-old" group is generally considered to be aged 65-74, while "middle-old" is 75-84, and "oldest-old" is over 85 years old.[1]

The percentage of the elderly population that is older than 70 years varies by country, but in the United States (US) those aged 75 and older make up about one-third of the > 65 years group according to a 2020 Census analysis. Globally, there is data showing that 43% of people worldwide now live past the age of 70 years.[2,3]

Healthy men aged 70-75 years in developed countries have an additional 12 to 14 years of life expectancy.[4] Given these trends toward a considerably longer life expectancy, a logical question arises whether ≥70-75 years old should be screened for high grade prostate cancer (PC) and then be offered radical treatment; and if so, under which circumstances?

One of the main criticism about the use of the PSA as a population screening test is that over detection often associated with lead time bias and length time bias, promotes unnecessary radical treatments which leads to urinary incontinence and various types of sexual problems, mainly loss erectile function not amenable to phosphodiesterase inhibitors, which negatively impacts the quality of life, due to the findings of low-risk cancers that will never become clinically significant in that man's lifespan.

Therefore, guidelines from several health organizations recommend against routine PSA screening tests for men over 70 years of age. The U.S. Preventive Services Task Force (USPSTF) says that for men aged 55 to 69 years, the decision to undergo PSA based screening for should be an individual one but should not be done after that. Also, "*men should have an opportunity to discuss the potential benefits and harms of screening and to incorporate their values and preferences in the decision*".[5]

The current 2023 American Urological Association (AUA) recommendation states that clinicians may decide to discontinue screening, based on patient preference, age, PSA, prostate cancer risk, life expectancy, and general health following shared decision making. Although the guideline states that clinicians should start with a baseline PSA between ages 45 to 50 years and should offer regular PC screening every 2 to 4 years to people aged 50 to 69 years, it does not clearly state when to actually stop testing.[6]

The European Association of Urology (EAU) has also moved away from imposing a strict age cut-off and instead now recommends that physicians take into account the patient's general health status and competing mortality risks when deciding whether to screen, emphasizing the use of risk calculators, MRI scans and genetic tests, potentially avoiding unnecessary radical procedures for low-risk cancers.[7]

The recently updated findings from the European randomized prostate screening program (ERSPC), a multicenter study of 162 236 men between 55 to 74 years (core age group: 55-69 years) demonstrated that after a median follow-up of 23 years, the PC mortality was 13% lower in the screening group, confirming a reduction in deaths from PC-with PSA testing.[8]

In the Goteborg screening study of 20 000 men born between 1930 and 1944, randomized to either a screening group with PSA testing every 2 years (n=10 000) or to a control group (n=10 000), after a median follow-up of 18 years the PC specific survival was 94%. However, the overall survival rate at 25 years for all men was 32%, demonstrating major competitive causes of death for this group of patients.[9]

Conversely, the percentage of clinically significant PC prostate cancer (Gleason score > 7) among men aged 70-74 is 22%, rising close to 40% for those close to 80 years of age. Among men ≥ 70 years, the incidence of high-risk disease (Gleason score 8-10 or PSA > 20 ng/mL or clinical stage T3/T4 or combinations) can be as high as 61%.[10,11]

For low-risk disease no survival benefit from intervention compared to active surveillance has been identified. However, clinicians may still undertreat older men with high-risk disease. The 15-year mortality rate from untreated high-risk PC is 55% compared to 22% from intermediate risk disease.[12]

How this could be done?

First, a comprehensive geriatric assessment is necessary to identify the healthy elderly and potentially reverse minor conditions which may interfere with PC screening, specially hypogonadism. Androgen levels are of highest importance because some PC cells may have been living in a low testosterone environment and by the time PC is recognized, a castration resistant prostate cancer status may be present with its adverse clinical consequences.

Secondly, the clinician shall take into account not only the total PSA and free to total percentage but should also incorporate other PSA calculations to improve PSA accuracy. Not an easy task. Total

PSA values measurements can fluctuate by up to 20-40% daily and is 10-30% lower when measured in the morning. Bicycling and similar exercises should not be forgotten.[13,14]

Two other important measurements are the PSA density (PSA-D) and PSA velocity (PSA-V). PSA-D relates to PSA and prostate size and should inferior to 15% (0.15 – PSA value divided by the gland volume measured by any form of imaging).

PSA-V is related to prostate grow, a more difficult issue because PSA values also relate to BPH. An acceptable PSA-V change is 0.75 per year but a higher value may be in order for the healthy elderly even though BPH doubling time kinetics after 70 years of age slows down considerable, over 1o times slower.[15,16]

Thirdly, prostate MRI is an important tool when PSA values are considered abnormal. Quality of the exam is critical and must be performed by well experienced radiologists when providing PIRADS v.2 data, especially when hip replacement surgery exists. Only PIRADS 5 (large visible nodules) and perhaps PIRADS 4 (< 1.5 cm nodule visible; 50% chance of cancer; 1/3 chance of being high risk) should prompt the decision to perform a biopsy, differently from the average adult recommendations, because studies have documented that PIRADS 5 scores are mostly related to aggressive PC (Gleason scores 8-10), thus avoiding the finding of lower grades tumors with lower PIRADS, a cause of unnecessary personal and family distress.[17,18]

Fourthly, a pet PSMA scan should also be incorporated in the decision process because it is capable of identify and stratify high risk PC much better than conventional imaging, even a low PSA value. An added benefit of the pet PSMA is relates to max SUV; low values, usually below 10-12, are predictive of low-risk disease.[19,20]

And finally incorporating genetic analysis of somatic and germline mutations such as BRCA2, BCRA1, ATM is becoming increasingly important. The presence of BCRA2 mutations are related to the development of aggressive PC and we have target therapies such as PARP inhibitors in addition to conventional treatment for such cases. Current genetic recommendations for the elderly are lacking.[21,22]

In conclusion there is a lack of consensus guidelines for PC PSA-based screening for the group of elderly patients with an ever longer life expectancy. They must incorporate functional status, patient preferences and include new tests for risk adapted strategies aiming at diagnosing only high-risk PC.[23,24]

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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