

Elderly and Prostate Cancer Screening

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Purpose: To discuss the issue of screening for prostate cancer in elderly individuals. The impact of life expectancy on the choice of treatment in both patients and health care providers has been investigated as well.

Materials and Methods: We identified studies published from 1990 onwards by searching the MEDLINE database of the National Library of Medicine. Initial search terms were “localized prostate cancer” and “early stage prostate cancer” combined with “elderly patients, life expectancy, palliative, curative, quality of life, watchful waiting, radical prostatectomy, brachytherapy, and external beam radiotherapy”.

Results: Despite the decrease in prostate carcinoma-specific mortality, the use of prostate-specific antigen (PSA) has been shown to increase the prostate cancer detection rate with a shift to detection at earlier and less invasive pathological stages, overriding concerns about over-diagnosis and over-treating. However, PSA screening is mainly offered to younger individuals, and older patients are more likely to have progressive disease and high-risk prostate cancer at diagnosis. Given that PSA screening diagnoses mainly curable, early prostate cancer, screening decision could be offered to otherwise healthy elderly patients who are likely to benefit from aggressive treatment.

Conclusion: Prostate-specific antigen screening is not officially recommended and most scientific associations promote shared decision making. While PSA screening decision is currently based on physician’s judgment, it is clear that a strict age cut-off of 75 years reduces over-screening, but also prohibits screening in healthy older men with a long life expectancy.

Keywords: prostate cancer, aged, prostate-specific antigen, life expectancy

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INTRODUCTION

A definitive cause of prostate cancer (PC) has not been identified and the specific mechanisms that lead to development of the disease are still unknown.⁽¹⁾ Although several risk factors have been proposed, the only ones that can be considered established are age, race, and family history.

Currently, it is not known how ageing facilitates PC development; however, this association may be mediated through androgenic action. On one hand, development

and function of the prostate gland are endocrine-controlled and androgen/estrogen synergism is necessary for the integrity of the normal human prostate. On the other hand, androgen action is critical to the development, progression, and cure of PC. Actually, androgens undergo a significant age-dependent alteration. With ageing, the production of testosterone by the testes is decreasing, leading thus to a significant reduction in the endogenous testosterone levels.

Dihydrotestosterone (DHT) activity decreases in the epithelium while it remains constant in the stroma over the whole age range.⁽²⁾ The age-dependent decrease in the DHT accumulation in the epithelium and the concomitant increase in the estrogen accumulation in the stroma lead to a tremendous increase of the estrogen/androgen ratio in the human prostate. Although the specific pathway remains partially investigated, it is widely accepted that these alterations promote the initiation of neoplastic lesions.⁽³⁾

Actually, PC is a disease of the elderly and its incidence increases with age. It seldom develops before the age of 40 and is chiefly a disease found in men over the age of 65 years. Furthermore, epidemiological evidence from autopsy studies shows that a high percentage of the elderly men has histological evidence of the disease.⁽⁴⁾ The aim of the present study is to discuss the issue of screening for PC in elderly individuals. A secondary aim is to examine whether or not advanced age impacts on PC risk. The impact of life expectancy on the choice of treatment in both patients and health care providers has also been investigated.

MATERIALS AND METHODS

We identified studies published from 1990 onwards by searching the MEDLINE database of the National Library of Medicine. Initial search terms were “localized prostate cancer” and “early stage prostate cancer” combined with “elderly patients, life expectancy, palliative, curative, quality of life, watchful waiting, radical prostatectomy, brachytherapy, and external beam radiotherapy”. References in the selected publications were checked for relevant publications not included in the MEDLINE or PubMed search.

RESULTS

Achievements in the 20th century, such as decline in mortality at younger ages, medical advances, and better health care, have resulted in longer life expectancy in both the developing and the developed world.⁽⁵⁾ Statistics compiled by the United Nations showed that in 1999, 10% of the world population was 60 years and older. By 2050,

this percentage will rise to 22%. In Hong Kong, where the proportion of elderly is even higher, it is estimated to rise to 40%.⁽⁶⁾ Regarding male gender, the population over 65 years is expected to increase 4-fold worldwide by 2050.⁽⁷⁾ The increased life expectancy enjoyed by the world population also means that the life span beyond the age of 60 is much longer than demographers have previously envisaged. A large proportion of the population remains active beyond the age of 70 and lives beyond the age of 80.

Changes in the world’s demographic proportions and introduction of the prostate-specific antigen (PSA) blood test in the last three decades altered the epidemiology of PC, which still remains a disease of the elderly.⁽⁸⁾ Prostate cancer is the second most frequent malignant disease in men and the most commonly diagnosed cancer in elderly men.⁽⁹⁾ Due to the steadily growing ageing population, the number of elderly men who will be diagnosed with PC and those who will require treatment will further increase in the coming years.⁽¹⁰⁾ While the majority of elderly patients with PC in the past were diagnosed with the advanced or metastatic disease, a rising number of elderly men are now diagnosed with early stage of PC. It is not known whether this is due to the effective utilization of health care resources or to the use of PSA testing.

At the moment, PSA screening is being performed unofficially in elderly patients. The magnitude of this opportunistic screening is not known. Hoffman and associates and Walter and colleagues found a 56% and 50% PSA screening rate in their cohort of elderly men in 2003 and 2010, respectively.^(11,12) Interestingly, Bowen and coworkers found that PC screening rates among men at the age of 80 and older are even higher than that of men in the age range of 50 to 64 years (64% versus 56%).⁽¹³⁾ Similarly, in the study by D’Ambrosio and colleagues, the highest yearly exposure to PSA screening (55%) and the highest frequency of repeat testing were observed in the age range of 70 to the 79 years. According to these authors, PSA screening practice has continued to increase in Italy and is often performed in elderly people without any scientific rationale.⁽¹⁴⁾ In contrast, Zeliadt and associates demonstrated that

PSA testing among men older than 75 years has declined slightly following the recommendations by the US Preventive Services Task Force in 2008 and is still continuing to decline.⁽¹⁵⁾

Several studies showed an eventual increase in the PC detection rate and a shift towards earlier pathological stage and less invasive forms, not without justifiable concern about over-diagnosis and over-treating.^(16,17) This fact is of outmost importance when deciding to treat elderly patients with PC. Given that life expectancy of American men at the age of 65 is 16 years⁽¹⁸⁾ and the mean time to cancer-specific death of apparently clinically localized low risk prostate cancer is 17 years,⁽¹⁹⁾ it becomes obvious why PC screening and treatment of PSA-detected PCs in elderly patients are very controversial issues.

On the other hand, evidence suggests that PSA may be useful in diagnosis of aggressive early PC in a subset of elderly patients. A current study by Brassell and colleagues demonstrated that as men age, parameters consistent with more aggressive disease become more prevalent.⁽²⁰⁾ Autopsy studies showed that a proportion of elderly men with histologically apparent disease may develop lethal PC.⁽²¹⁾ In fact, most of these cancers are likely to progress and become clinically significant (advanced Gleason score and greater volume) and therefore it is not surprising that older individuals with clinically apparent PC usually die from PC. It is noticeable that these two clinical (age-related) forms of the PC are still undistinguishable in clinicopathology reports.⁽²²⁾ These data may have implications for future screening and treatment recommendations since currently, patients bearing different diseases are offered the same treatment.

Currently, age plays an important role in treatment choice and thus elderly patients are less likely to receive local therapy. In fact, only a small number of elderly patients with early stage of PC are treated with intent to cure. Despite the limited data, there is clear evidence of survival benefit in several elderly patients receiving radical treatment.^(23,24) Given that PSA screening mainly diagnoses early PC, it may be justifiable for otherwise healthy elderly men to undergo PSA test. This is of outmost importance since

older patients are more likely to have high-risk prostate cancer at diagnosis and lower overall survival. In fact, under-use of potentially curative local therapy among older men with high-risk disease may explain, at least in part, the observed differences in cancer-specific survival across age strata.⁽²⁵⁾

To the best of our knowledge, global PC mortality is constantly decreasing. As yet it is not possible to say what proportion of the fall in mortality is the result of improvement in treatment, changes in cancer registration coding, the attribution of death to PC, and the effects of PSA testing. Accumulative evidence, however, suggests that early screening of PC in asymptomatic men reduces risk of death from metastatic disease. Interestingly, the recently published results of the European Randomized Study for Screening of Prostate Cancer reported a relative PC mortality reduction of at least 20% by PSA-based population screening⁽²⁶⁾ while Kopec and colleagues reported a relatively high risk of death from metastatic PC among men who were not screened regularly as part of a screening program.⁽²⁷⁾ On the other hand, data from US Cancer of the Prostate Strategic Urological Research Endeavor showed a significant reduction in risk of death from metastatic PC in the last two decades in the US, with most of the patients being found with low or intermediate disease at diagnosis.⁽²⁸⁾

Taking in consideration these findings along with observations of Brassell and coworkers,⁽²⁰⁾ it became obvious that evidence supports making decisions regarding screening and treatment on the basis of disease risk and life expectancy rather than chronologic age.

To our knowledge, no standard recommendation for PC screening exists. Recently, the American Urological Association recommends PC screening to men aged 40 years or older. In contrast, screening is presently discouraged by the European Commission Advisory Committee on Cancer Prevention for its negative effects are evident and its benefits are still uncertain.⁽²⁹⁾ According to the U.S. Preventive Services Task Force, evidence is insufficient to recommend in favour of or against routine PC screening.⁽¹²⁾

On the other hand, treatment recommendations are now recognizing that older men with PC should be managed according to their individual health status, which is mainly driven by the severity of associated comorbid conditions, and not according to chronological age. According to the International Society of Geriatric Oncology Prostate Cancer Task Force, it is possible, based on a rapid and simple evaluation, to classify patients into four different groups: 1) “Healthy” patients (controlled comorbidity, fully independent in daily living activities, and no malnutrition) should receive the same treatment as younger patients; 2) “Vulnerable” patients (reversible impairment) should receive standard treatment after medical intervention; 3) “Frail” patients (irreversible impairment) should receive adapted treatment; 4) Patients who are “too sick” with “terminal illness” should receive only symptomatic palliative treatment.⁽³⁰⁾ The same rapid and simple evaluation may help physicians who perform PSA screening to decide who to screen.

CONCLUSION

Evidence supports serum evaluation of PSA for screening of prostate cancer in elderly individuals. A strict age cut-off of 75 years reduces over screening, but also prohibits screening in healthy older men with a long life expectancy who may benefit from screening. Therefore, recommendations for PC screening in the elderly individuals should be based upon health status and life expectancy. Certainly, physicians who perform PSA screening should maintain sound clinical acumen and judgment when deciding who to screen.

CONFLICT OF INTEREST

None declared.

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