Prostate Cancer Screening, Yes or No? 
the Current Controversy

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ABSTRACT

Purpose: The increasing incidence of prostate cancer and different viewpoints of medical authorities to it, has lead to conversion of preliminary plan of screening test to a requisite. The objective of this study is to clarify the obscure aspects of this subject using the literature review.

Materials and Methods: We reviewed the following items in the literature: prostate cancer screening, introduction of relevant tests, screening criteria according to World Health Organization, screening experience in different countries, community notification, specialists training in order to establish an integrated approach and treatment, anxiety relief, and promotion of patient awareness in this field.

Results: It has been shown that, except in China, programmed and official screening of prostatic cancer has not been accepted by concordant responsible authorities, neither in developed countries nor in developing ones. However, it is performed informally in different parts of the world.

Conclusion: There is no unanimous consensus about performance of screening for prostate cancer. Continuing voluntary referral of men above 50 years old for performing prostatic specific antigen (PSA) test has been accepted universally and is being done potentially, defined as "opportunistic screening".

KEY WORDS: prostate cancer, screening, incidence

Introduction

Prostate cancer is a universal and serious health threatening disease. It is seen mainly in the aged and its occurrence is very rare under the age 50. Its incidence has increased significantly in the recent years, but its mortality has not followed this trend. It might be due to physicians' attention to this disease, its diagnosis in early stages, and appropriate treatments. Some authorities believe that this success is indebted to performance of prostatic specific antigen (PSA) test.(1,2)

Prostate cancer is the most common malignancy, diagnosed in the United States and generally in western men.(3,4) Although in some reports it has the second rank after skin cancer, it is the second cause of death from malignancy. Factors such as a positive family history, black race, and the presence of prostate intraepithelial neoplasia in previous biopsies increase the risk of its occurrence.(2,5)

It has been observed that the chance of positive results of malignancy in the performed biopsies is increasing in young age group. For instance, in one study in the United States the rate of diagnosed prostate cancer by biopsy in patients aged 50 to 59 years has increased from 11% in 1995 to 16% in 2002; whereas, in those of 70 to 74 years old, this rate has declined from 46% in 1995 to 34% in 2004.(6)

These studies show that the need for performing screening test has converted to a requisite, specially due to increment in education level and awareness of population and improvement in their socioeconomic status, their request to do screening test has increased. Although it is rarely seen that the health service of a country accepts screening test for prostatic cancer as a health policy, the opposite is happening in the world; the
daily rate of PSA tests performed indicates informal performance of this test despite compile programs, and free referral of people to do these tests confirms their acceptance.\(^{(7)}\)

There is another point that, a large distance has been created between opinion and action due to high demands for these tests. In theory, at present, there is a unanimous consensus not to perform PSA test for patients over 75 years old, due to accepted reasons. The high incidence of histological cancer, low life-expectancy, and the presence of co-morbidities, of which, some are more fatal in this age group, has lead to this agreement.\(^{(7)}\) However, for these patients, PSA test is practically done according to patient demand and physician's recommendation. For example, in a national research in 2000 in the United States, 7889 old men were interviewed, showing that 34% had done PSA test after the age 75 years old, of which 86% was due to physician's recommendation and in 12%, patient's demand was involved.\(^{(8)}\) This rate is comparable to the rate of pap smear application for cervical cancer in females, but less than that of stool occult blood test for colorectal carcinoma.\(^{(8)}\) On the other hand, at least there is no consensus that screening test can affect present treatment and subsequently, mortality and morbidity due to prostate cancer\(^{(7,9,10-13)}\) and also there is no consensus that early diagnosis of the disease reduces early mortality. At present, 3% of mortality rate in western men over 55 is due to this disease.\(^{(4)}\)

Some authorities believe that screening test is even harmful, because it may disclose those tumors which might never become clinically considerable, otherwise, patient will dye "with" the disease, not "of" the disease and if diagnosed, the patient will suffer from being aware of his illness and should undergo different stages of investigation and treatment, which might be accompanied by significant morbidities (i.e. incontinency, impotency, intestinal complications, etc.).\(^{(2,14-17)}\) Accordingly, they reserve PSA test until obtaining a written informed consent from the patient\(^{(13)}\) and not a verbal one. In the other end of the spectrum, some believe that not performing this test may increase a serious risk of reducing longevity and quality of life in men. In a study done in Quebec, Canada, it has been shown that mortality rate due to prostate cancer in screened group is one third of that in controls.\(^{(14)}\)

On the other hand, the sight of society and asking for screening is understandable; people believe that the same level of care for breast or cervical cancer in females should be done for malignancies in males, as mammography, pap smear, or ultrasonography in normal pregnancies are routinely done in some countries worldwide, such as Belgium, the Netherlands, Japan, Australia, the United States, etc.\(^{(16,18-20)}\) Finally, as we enter the post-genomic century, introducing biomarkers and molecular-based prognostic markers will clarify PSA test obscurities and identifies those patients who have a great potential for malignancy, so that the story of screening test will get more evident.

Who is responsible for screening tests?

Is World Health Organization (WHO) responsible or ministry of health, medial professionals such as specialists or general practitioners, or medical universities? Actually, in Iran, it seems that urologists, despite ministry of health and universities' responsibility, informally should undertake this duty and accompany people's will.

Which types of screening are being performed?

There are different types of screening, performing for different diseases and each of them has its own condition.

1- Mass Screening: In this type of screening which is performed in a specific population or group, the goal is to detect the disease in its primary stage, when the treatment is practically most viable.\(^{(2)}\)

2- Selected Screening: It is a screening of a selected group of people such as those who are placed in a high-risk category (positive family history, black race, etc.)\(^{(1,2,5)}\)

3- Case Finding: This type of screening, which is done in periodic check-ups (each 6 months or 12 months), is based on an obligation. For example, a person who is employee in an organization is to participate in periodic obligatory check-up programs and give his/her health reports to the system.\(^{(2)}\)

4- Opportunistic Screening: It refers to a situation in which the physician uses any opportunity to perform screening test. The request for performing this test is based on physician's preference or patient's willingness.\(^{(2)}\)

All the above-mentioned methods are used in the management of prostate cancer, but the opportunistic screening is more common.\(^{(14,16,18-20)}\)
WHO Criteria For Screening Tests

WHO has specified a series of criteria for performing screening tests in the management of any disease:(2)
1- The target disease should pose as a health problem.
2- The latent form of the disease or at least its clinical form in early stages should be diagnosable.
3- The natural history of the disease and its transition from latent to clinical form should be known.
4- There should be acceptable treatment for those who are diagnosed.
5- There should be known laboratory test and physical examination for diagnosing the disease.
6- The test should be accepted by the community.
7- There should be an approved policy (or unanimous strategy) for the treatment of patients.
8- Available facilities for diagnosis and treatment should be present.
9- Case finding expenses should be equivalent to medical care expenses.
10-Case finding process should be consistent.

Adaptation of WHO criteria for prostate cancer

It is believed that screening test for prostate cancer has some concordances and incongruities as compared to WHO criteria:
1- The disease should pose a health problem: This is true for prostate cancer. The incidence of disease is increasing, but first, the mortality and morbidity rates have remained constant and second, the disease belongs to old ages and if it is not screened, the danger for the patient is less than that of lung, colorectal, and breast carcinoma.(1,2,14,20-22) It means that the priority is not given to prostate cancer.
2- The latent form of the disease or at least its clinical form in early stages should be diagnosable: Although we are able to diagnose the latent form of prostate cancer, we are unable to differentiate the non-progressive disease from its fatal form.(1,7,12,14,16,23) Prostate cancer has a low fatal potency. Many of the patients die of other diseases rather than prostate cancer. It is probable that screening test may diagnose a benign form of disease, not requiring treatment, which will impose unnecessary measures on patients.(1,5,8,11,15,16,23)
3- The natural history of the disease and its transition from latent to clinical form should be known: There is not much information about the nature of prostatic cancer and the studies performed in this filed has not achieved definite results. Despite the broad studies, which have been performed on age, nutritional regimen, body mass, physical status, genetic factors, and vasectomy, the risk factors of prostate cancer are not known yet.(1,2,20)
4- There should be acceptable treatment for those who are diagnosed: Although there are acceptable treatments such as radical prostatectomy, radiotherapy, and watchful-waiting available for prostate cancer, there is a question whether these treatments will alter the natural course of preclinical disease or not, which is not answered yet. Radical prostatectomy for organ confined form of the disease is the best treatment, but nobody has used the term "treatment of choice" for it. Some advocate radiotherapy, specially in old patients. But, both of these treatments have complications such as urethral stenosis, injury to intestine, incontinency, and impotence, which are intolerable and problematic for those patients who have the histological form of the disease, but not its clinical form. Robeca Ferrini, a member of the American College of Preventive Medicine, refers to these as a reason for objection to screening tests.(1)
Watchful-waiting, although not an active treatment, is accepted as a treatment strategy, in those patients who are monitored closely and any treatment is aimed to appearance of the signs of disease. The mean time from diagnosis to the need for treatment is 10 years, making the early treatment of prostate cancer questionable.(2)
5- There should be known laboratory and physical examinations for diagnosing the disease: Digital Rectal Examination (DRE) test has been being used for a long time, but it is helpful in diagnosis of the palpable form of disease and the result of test is different among physicians. The sensitivity of test is different from 18% to 68%, which is due to the different sensitivity of examiners' fingers.(1,2)
In a study, it has been shown that one case of
prostate cancer is detected in each 96 rectal examinations, which might not be a clinically significant form, and 289 rectal examinations should be performed to diagnose one case of clinically significant prostate cancer.(24)

The principal screening test for prostate cancer is PSA test, which was discovered in 1979 and could make a revolution in early diagnosis of the disease, otherwise known as PSA-Era or PSA revolution. However, there is high variation in sensitivity and specificity.(2,25,26) Its sensitivity is 27% to 80%, being higher for aggressive cancers. Its cut-off point value is controversial and although 4 ng/ml is acceptable, the amount of 4.1-10 ng/ml is considered as Gray Zone by all authorities. There are different cut-off points in different parts of the world; in Japan, those with PSA<2 ng/ml are excluded from annual control(28) and in the United States, some believe that the cut-off point should be PSA=2.5 ng/ml. However, measurement of free PSA, age adjustment, and determination of PSA velocity and PSA density can help to determine the cut-off point. Performing biopsy in those with a PSA between 4.1 and 10 ng/ml will lead to diagnosis of cancer in 25%. (29)

Finally, PSA is accompanied with high false positive results, which its psychological burden would be a matter of attention and it is necessary for the results to be confirmed with second line tests such as transrectal ultrasound (TRUS) or transrectal ultrasound-guided biopsy (TRUS-GB). But these tests are invasive and can not be used as a screening test; whereas, PSA is eligible to be a screening test according to WHO criteria.(2,16)

6- The test should be accepted by the community: There is no study regarding the community acceptance and to show how much the people are satisfied with screening test, but in many communities such as the Iranian, the patients have embarrassment with DRE and the cost of PSA may be high for some patients.

7- There should be an approved policy for the treatment of patients: There is no such agreement about prostate cancer. In addition there is no agreement that early diagnosis can reduce mortality rate with appropriate treatment. Two large randomized and multicenter study in the United States and Europe are in process, publishing the results in the future.(2)

In a study done in Quebec, Canada, 80137 men above 50 years old underwent DRE and PSA. In case of abnormal results for each test, TRUS was performed and in doubtful cases, biopsy was done. These patients were compared with 38000 unscreened controls. The mortality rate from prostate cancer decreased dramatically in screened patients (5/100000 vs. 48.7/100000). There are also many studies such as the one done by Barry and colleagues from Massachusetts hospital, that disagrees the above. They believe that there is no study that confirms the role of prostate cancer screening in reducing mortality and morbidity of the cancer. Although over-treatment is not always associated with increased mortality, unawareness of benefits and harms of invasive treatment of patients diagnosed via screening and its high cost should be taken into account.(23)

8- Available facilities for diagnosis and treatment should be present: Certainly, performance of screening test for prostate cancer needs more facilities and human and financial resources, which is not enough at the moment.

9- Case finding expenses should be equivalent to medical care expenses: It is not true for prostate cancer because expenses comprise both human and financial resources and screening expenditure is much higher than medical care expenses. Mass screening is estimated to cost 12 to 28 billion dollars in the United States, that means such equilibrium is not present.(1)

10- Case finding process should be consistent: Due to constant dispute about screening test in prostate cancer,(7,9,10-13) time intervals for its performance have not been determined. As a result screening test for prostate cancer is not concordant with WHO criteria and it is not documented whether it can improve the health condition of the population or not. Hence, screening test for prostate cancer may not be introduced formally, but its opportunistic form which is now performed in practice, can be justified.

How is the screening status in different countries?

The United states

Prostate cancer is the second most commonly diagnosed malignancy after skin cancer and the
second most common cause of death due to malignancy after lung cancer. There is one death for each five diagnosed prostate cancer annually.\(^{(1)}\)

The opportunistic form of screening is performed in this country. It means that the patients who demand to perform this test themselves and those who refer for other prostatic disease such as BPH are evaluated and among the tests, DRE and PSA are performed as the first line tests and TRUS and biopsy are in the second line for those whose one or both test results are abnormal. American Urological Association (AUA) and American Council of Radiology (ACR) have advised that all men above 50 years old should undergo PSA test and DRE annually and for high risk and Afro-American men it should be performed at 40 years old. American Cancer Association has limited these tests to those who have at least 10-year life expectancy.\(^{(1)}\)

But American College of Physicians (ACP) and Office of Technologic Assessment (OTA) object to annual follow-up and believe that people should be informed, so that they decide themselves.

In summary, the United States Preventive Service Task Force (USPSTF), who is responsible for general examination in regular periods is against screening for prostate cancer and believes that there is not enough evidence in favor of or against screening and because of few reports on effectiveness of early intervention in prostate cancer, there is no reason to expose the patients to factors such as anxiety, biopsy and complications of treatment.\(^{(1)}\)

The Netherlands

In the Netherlands, preventive medicine takes priority in the government’s point of view and Health Technology Assessment (HTA) is of special importance. Based on this country’s rules, which is unique all over the world, screening test should be thoroughly investigated and its efficacy and ethical, legal and social aspects should be considered. Researchers and experts have performed studies on PSA test for prostate cancer, mammography for breast cancer, and ultrasonography for normal pregnancies as screening tests. Different studies has led to acceptance of mammography, but for screening with PSA and ultrasonography only their opportunistic forms are accepted.\(^{(15)}\)

Belgium

Numerous studies have been performed regarding PSA for prostate cancer, mammography for breast cancer, and ultrasonography for normal pregnancies in Belgium. Published articles, performed researches, unpublished manuscripts and different interviews with experts have been reviewed. As a result, only in Flandre area mammography is being used as screening for breast cancer and a final agreement is not reached for other screening tests.\(^{(20)}\)

Australia

Australian Health Technology Advisory Committee (AHTAC) has performed an extensive study on advantages, risks, and costs of screening for prostate cancer. They concluded that it can not be recommended and only opportunistic screening has been advised and supported.\(^{(2)}\)

Austria

Only opportunistic screening has been accepted in this country.\(^{(29)}\)

China

Mass screening for men above 50 years old is performed in this country and they believe that, it is the only way to diagnose the disease in its early stages.\(^{(30)}\)

New Zealand

Although screening with PSA test has not been accepted and is not performed in this country, many of male population without signs or symptoms are referred for PSA test and DRE. However, this rate is less than that in Australia.\(^{(31)}\)

Need for Educational Programs and Ethical Consideration

There is no doubt that there is not any consensus regarding screening test for prostate cancer. On the other hand, it is a health problem and there is a general demand in this regard. Therefore, it is necessary that the problem should be clarified for the society, medical professionals, and responsible organizations through an educational program.

Prostate Disease Patient Outcome Research Team (PDPDRT) in the United States has accepted the responsibility to prepare appropriate educational material for physicians and patients. An educational pamphlet, which provides complete information, is distributed widely among people and medical professionals are educated via continuous medical education program.

In addition, ethical burden resulted from screening tests should also be considered and enough care must be taken to that the result of screening does not affect employment or insur-
ance facilities for immigrants.

**Conclusion**

PSA screening test cannot be imposed to the health system of a country as a complied program. People’s demand for performing PSA test and available opportunities should definitely be used for its performance.

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