Editorial

Screening for prostate cancer: what are the benefits?

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In men of advanced age, the epithelial cells of the prostate gland undergo substantial stress-associated changes that may result in DNA damage. The aging prostate gland acquires several cancer cell foci originating from special clonal transformation. Most of these foci never develop into clinically detectable cancer.(1)

In the United States, prostate cancer ranks second as the cause of death of all cancers affecting men. With the increasing use of screening for prostate-spesific antigen (PSA), the mortality rate from prostate cancer has decreased. For example, the mortality rate in 1997 was far below that recorded for 1986 when PSA tests were seldom performed.

There is a consensus of opinion among clinicians that the PSA test has the highest predictive value for prostate cancer, and that PSA screening may help detect prostate cancer in its early stages. However, there is no consensus on the level of PSA that may be used as an indicator for performing biopsy. This difference in opinion is based on the following: defining a higher PSA threshold carries the risk of loss of the probability of detecting prostate cancer until too late, while a lower threshold unnecessarily increases such measures as biopsies. The use of a PSA threshold value of 4.0 ng/mL for men older than 50 years has been accepted by most clinicians as a middle way for the above issue. However, there is a lack of information on the prevalence of prostate cancer detectable by biopsy among persons with a PSA value of $\geq$ 4.0 ng/mL without indications for biopsy.(2)

Recently the U.S. Preventive Services Task Force (USPSTF) has issued a recommendation statement against the use of PSA tests as the basis for prostate cancer screening, after this test had been extensively applied for that purpose in the last couple of decades.(3) All guidelines recommend that clinicians discuss beforehand with the patients the advantages and disadvantages of this test and to leave the decision to the patients individually in accordance with their choice. To help the patients make their choice, clinicians are recommended to provide information on the uncertainties and risks, in addition to the potential benefits of this test. Among the benefits may be that screening may lead to early detection of prostate cancer, whereas one of the risks is that screening may result in serious complications for the patients due to the effect of interventions. However, for both clinicians and patients, it is not easy to reach a decision on this issue, because it includes a number of unanswered possibilities, for example, what is the best cut-off point for PSA? At which concentration or value is it considered necessary to perform repeat PSA tests, or is there a need for performing biopsy? Should a repeat test be indicated, when should it be performed? How high is the probability that PSA tests in combination with biopsy can detect cancer, assuming the existence of prostate cancer? The most important question is: can screening

reduce the risk of death from prostate cancer? Because of the high number of possibilities evaluated on the pros and contras, reaching informed decisions may be said to be difficult; as most of these decisions reflect the patients' general concern about cancer or their inclination to accept (or reject) medical intervention.[4] Since 2009, clinicians' considerations about the need for performing PSA tests are becoming increasingly more difficult to deal with, because of the indefinite results of 2 large studies and the fact that experts in this field are still not agreed on their interpretation.[5] Discussion with patients on the advantages and disadvantages of PSA tests has becomes increasingly more difficult, because now clinicians must explain to patients why there is uncertainty about the results of PSA screening and why two large studies are still incapable of providng certainty.

Another variable causing problems is the management of PSA values in primary health care. Many PSA values are near the threshold commonly used to determine measures, this being in the range of 2.5 – 4.0 ng per mL. The patients are then to be retested a number of times at arbitrary intervals. Frequently cven the increase in PSA values causes the patients to be prescribed quinolones that are intended to reduce the PSA values in these asymptomatic patients who are assumed to have prostatitis. These attitudes reflect either a fundamental misunderstanding or an unwillingness to accept the limitations of the PSA test as a marker for early detection of prostate cancer.

Observational studies clearly indicate that PSA values fluctuate spontaneously above or below any threshold level, while random biopsies may detect prostate cancer in 12% of men with PSA values of < 2 ng/mL and in 25% of men whose PSA values are between 2.1 and 4.0 ng/mL. The latter percentage almost equals the prevalence of prostate cancer frequently found in men with PSA values of 4.0 – 10.0 ng/mL.

One problem that is of no less importance and is frequently ignored is the economic factor, i.e. the costs to be paid by individuals in connection with PSA screening. This includes repeat screenings in cases of equivocal PSA results or interpretation of fluctuating results of PSA screening. In addition the patients have to return many times to the clinicians for discussion of the equivocal test results. It is the required time and costs that frequently receive less attention in the management of PSA screening.

According to the European Randomized Study of Screening for Prostate Cancer (ERSPC) in estimating the risk of prostate cancer, the probability of finding cancer by biopsy is 21% in a 65-year old man who has decided to undergo biopsy on the basis of a PSA value of 4.0 ng/mL. If this man has a routine urological examination, comprising digital rectal examination (DRE) and estimation of prostatic volume by transrectal ultrasonography (TU) or other methods, the expected value of biopsy results changes dramatically. If a normal DRE is found without any suspicious lesions being found on TU, and the prostatic volume is 55 mL, the risk of a positive biopsy result decreases to 8%. If DRE and TU results are abnormal, even with a prostatic volume of 25 mL, the risk of positive biopsy is 65%. Therefore, inclusion of other results dramatically changes the indications for biopsy on the basis of PSA tests.

In view of the abovementioned factors, presumably the paradigm of PSA screening is less in step with the priorities of health management. Nevertheless, consideration for performing PSA screening PSA should not be ignored by assuming that it is of no benefit at all. However, the decision to perform PSA screening should be made individually by patients who are clearly informed and after discussing it with their physicians, with consideration of various relevant factors.

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