



September 2007

PROSTATE CANCER AND PSA TESTING

The availability of Serum Prostate Specific Antigen (PSA) testing in NSW since 1988 has been widely used in the community to detect possible prostate cancer in men over the age of 55 years. In the eight years following its availability, PSA testing has contributed to the 125% increase in the incidence rates of prostate cancer.

However, PSA testing should be used following discussion with a doctor. The test detects levels of a protein which is only indicative of the possible presence of prostate cancer, but may also indicate benign or non-malignant enlargement of the prostate or other non-cancer conditions such as infection. The test also cannot differentiate between an aggressive prostate cancer which could spread beyond the prostate, or a less aggressive tumour which may never cause harm.

A positive PSA test would usually lead to a recommendation to remove or treat the possible cancer. Such treatments may include radical surgery. Side effects occur in some patients and should be discussed with a doctor and can include erectile dysfunction, incontinence, bowel problems and the loss of bone density. Serious implications such as these may need to be discussed with the doctor when deciding to test or to treat a positive test. The prognosis of prostate cancer may differ and also needs to be discussed by the patient with their doctor.

This Cancer Institute NSW Position Statement provides the NSW community with information about prostate cancer, symptoms, risk factors, PSA testing and how PSA testing can be effective when coupled with other testing methods.

Mass-population routine screening of prostate cancer in asymptomatic men using PSA is not currently recommended because of a lack of medical evidence. Such recommendations would be reviewed when the results of current global clinical trials assessing the value of PSA screening are known.

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Prostate Cancer: Incidence and mortality

Prostate cancer is the most common registrable cancer and the second most common cause of cancer death in Australian men. Incidence and mortality increase with age. Prostate cancer is rare in men before the age of 50-54 years.¹

It is generally accepted that more men die with prostate cancer rather than from it, and more than 70% of cases are in men over the age of 65.

Survival appears to be directly related to tumour grade, with studies indicating disease-specific survival of 87% for grade 1 and 2 tumours and 34% for grade 3 lesions.²

It has also been shown that progression of the disease is linked to loss of differentiation, which is in turn, linked to increasing volume. The ability for these tumours to metastasise is associated with tumours that are larger than "1 ml" and have acquired poorly differentiated areas.²

In 2003 in Australia, 13,526 new cases of prostate cancer were diagnosed and 2,761 men died from this cancer. The incidence rate of prostate cancer is much higher in Australia compared to the UK and Europe, but is well below rates in the US and Canada.^{1,3}

In NSW, it is expected that 1 in 8 men will develop prostate cancer by the age of 75 years. In the ten years from 1995 to 2004 incidence rates for prostate cancer declined. In the past 10 years mortality rates have fallen by 22%. Survival five years post diagnosis is 88% in NSW.⁴

Natural history

Natural history of prostate cancer is varied. Prostate cancer can range from very aggressive tumours to slow growing tumours, which might never cause any harm. It is not always possible to predict the level of aggressiveness although the microscopic findings and degree of spread at diagnosis can give an indication.

Risk factors

The strongest risk factor is age with family history, ethnicity, diet, and hormonal influences playing some part.⁵⁻¹⁰

It has been shown that up to 15% of cases are inherited.⁵⁻⁶ People at high risk group are usually those with one or more first degree relative (father, brother, son) diagnosed before the age of 70.¹¹

Clinical features

Localised prostate cancer confined to local region is usually asymptomatic since it grows in the outer parts of the prostate gland. Symptoms such as pressure effect to the urethra or bladder usually indicate a late stage cancer by which time the cancer has metastasised.

Locally advanced prostate cancers extend outside the prostate capsule. These cancers are usually asymptomatic.

Metastasis, or when the cancer has spread beyond its origin, is usually when the evidence of prostate cancer becomes visible.

Prostate cancer detection

In Australia the incidence rate of prostate cancer increased dramatically between 1990 to 1994. The incidence rates fell by 30% between 1994 and 1997 and the rates since then have been steady.³ This fluctuation has been attributed to the introduction of PSA testing.

In NSW since the introduction of PSA around 1988 until 1994, the incidence rates rose by 125%. Since then the incidence rates have fallen to earlier levels.⁴

Serum Prostate Specific Antigen (PSA) testing from the blood is currently the most efficacious marker for the detection of prostate cancer. PSA is a protein produced by the prostate gland and it is thought to be involved in liquefaction of the seminal coagulum that is formed at ejaculation.

A serum PSA level of 4 ng/ml (cut-off level) or higher has been used to demonstrate the possible presence of prostate cancer. However, the level of PSA is not prostate cancer specific, and can be raised in a number of other circumstances, including benign enlargement of the prostate, prostatitis and urinary tract infection.

It is evident that as high as 27% of patients diagnosed with prostate cancer have PSA levels lower than "cut-off level".¹² Some researchers advise that the cut-off level needs to be lowered to 3 ng/ml.¹³

Of men with PSA levels of 4-10ng/ml, 25% have cancer, and 60% of those with PSA levels greater than 10ng/ml have cancer (World Cancer report 2003, p160). This situation is further complicated by the findings that PSA levels might be different among different races.²

Thus, it has become apparent that PSA as a single method of testing is not sufficient. Therefore, in common practice this method is combined with Digital Rectal Examination (DRE).¹⁴ Each as a single method misses some cancers but in combination they are more likely to be effective in detecting prostate cancer.¹⁵

High level of PSA and positive DRE is usually followed by Transrectal Ultrasound guided (TRUS) prostate biopsy. Approximately two thirds of men with elevated PSA levels are found to have negative biopsy results. This is complicated by the fact that up to 30% of negative biopsies on initial examination have cancer on repeated biopsies.¹⁶

Conclusion

Some organisations, such as the American Cancer Society and the American Urological Association, encourage the use of PSA and DRE as screening tests annually. These organisations have published guidelines advocating annual DRE and PSA testing for men over the age of 50 years, which is being practiced by many urologists. Some groups discourage against screening of men older than 75 years of age.¹⁷

Others however, recommend against prostate cancer screening, including the US National Cancer Institute and the Canadian Urological Association. In the UK, no organisation actively encourages its use but it is used on an *ad hoc* basis for men who request it.

Since the introduction of PSA rates of prostate cancers detected has increased. However, the results on mortality are conflicting.¹⁸⁻²⁰

It is apparent that in order for the current treatment modalities to have any value, the cancer must be detected at an early stage. Thus screening using PSA and DRE is potentially very valuable and can detect over 83% of localised cancers.²¹

However, currently it is impossible to precisely determine the aggressiveness of the disease using these screening tools, although pathology may assist some patients who may need less aggressive treatment especially for cancer that might never become aggressive.

There are currently two large randomised controlled trials being conducted, the European Randomised Study of Screening for Prostate Cancer (ERSPC) due for completion in 2008 and the United States Prostate, Lung, Colorectal and Ovarian Cancer Screening Trials (PLCO). Screening of participants in PLCO trials completed in 2006. These participants will be followed for a further 10 years to see if prostate screening has any benefit in reducing mortality. The results of these large randomised clinical trials hoped to shed more light into the issue of population screening for prostate cancer.

Another important study in the UK (ProtecT) opened for recruitment in 2001. This study will randomise men to surgery, radiotherapy or active monitoring (monitoring with regular check-up) with survival as an end point to be evaluated after 10 years. It is hoped that this study will provide "insight into PSA detection of early stage prostate cancer and its natural history".²²

Even if detected early in a localised state, the debate over the best treatment is still not settled. The National Health and Medical Research Council (NHMRC) recommends conducting well designed clinical trials exploring the effectiveness of currently competing treatment options and their long-term benefits versus no active treatment for localised tumours.

More conclusive evidence about optimal therapy is needed in early stage prostate cancer considering some of the side effects of treatment. Side effects of treatment include erectile dysfunction, urinary incontinence and bowel problems and loss of bone mineral density with androgen deprivation therapy resulting in one fracture out of 28 men treated.²³

The Cancer Institute NSW advises that population screening of prostate cancer in asymptomatic men using PSA is not yet established as a method for lowering mortality. PSA testing of high risk individuals is an option which needs to be discussed with patients who will ultimately make a decision after considering all the limitations and side effects of current methodologies.

The Cancer Institute NSW encourages all primary health care providers to discuss the advantages and disadvantages of current detection methodologies prior to conducting PSA testing in asymptomatic men. The main issue with current detection methodologies is the high level of false positives. This limiting drawback must be explained to all patients requesting prostate cancer detection.

The Cancer Institute NSW encourages uptake of healthy lifestyle habits in all men to reduce their risk of developing cancer. This includes intake of appropriate amount of fat, fruit and vegetables and exercising. Men should also limit their intake of alcohol and quit smoking.

The Cancer Institute NSW promotes these activities through the *Cancer Institute NSW Cancer Prevention Plan*.

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About the Cancer Institute NSW:

The Cancer Institute NSW is Australia's first State-wide Government cancer control agency. It was established in July 2003 through the Cancer Institute NSW Act 2003 to help further reduce the impact of cancer. The Cancer Institute NSW is responsible for reducing cancer incidence, increasing cancer survival, improving the quality of life for cancer patients and their carers and providing expert advice on cancer.