

Should you screen?

Cancer of the prostate is the most frequently diagnosed visceral cancer of men worldwide, including South Africa.



Dr Sudesh Naidoo

MBChB MMed Rad Onc (Wits)
FC Rad Onc (SA)

Specialist Radiation Oncologist

Director of the Ahmed
Kathrada Cancer Institute

Radiation Oncology Advisor to the
Ministerial Advisory Committee
on the Prevention and Control
of Cancer in South Africa

Dr Naidoo is affiliated with the More Balls Than Most NPO. "We're dedicated to promoting awareness about the importance of early detection of prostate and testicular cancer. More Balls Than Most is a cause marketing fundraisers (PBO number 930025386) initiative and is addressing the testicular and prostate cancer issue in South Africa by embarking on an awareness and fundraising campaigns."

According to the latest National Cancer Registry (NCR 2012), the number of cases diagnosed in that year was 6807. The estimated life time risk is 1:19 and makes-up 18,45% of all cancers diagnosed," said specialist radiation oncologist, Sudesh Naidoo.

The median age of diagnosis is 70 years, but with increased screening, more younger men are being diagnosed. The prostate gland consists of the peripheral zone (70% of glandular prostate and site of nearly all cancers), the central zone (25% of the glandular prostate), the transition zone (surrounding the urethra and the site of benign prostatic hypertrophy), and the anterior fibromuscular stroma.

"Approximately 50-80% of tumours involve the prostate apex, and around 85% of patients have multifocal disease in the prostate. More than 95% of prostate cancers are adenocarcinomas," said Naidoo.

Potential risk factors

- » Advanced age
- » Benign prostatic hypertrophy
- » Diet e.g. high-fat intake
- » Family history of prostate cancer – frequency of prostate cancer, increases with family history of first degree relatives with prostate cancer.
- » Hormonal factors e.g serum testosterone and androgens are required for the development of prostate cancer
- » Race /ethnicity e.g Black.

Is screening still relevant?

"A screening programme could accurately identify asymptomatic men with aggressive localised tumours, might be expected to substantially reduce prostate cancer morbidity, including urinary obstruction and painful metastases, and mortality," said Naidoo.

However, prostate cancer screening has been a controversial issue because decisions were made about adopting PSA testing in the absence of efficacy data from randomised trials. Subsequently, the European Randomised Study of Screening for Prostate Cancer (ERSPC) reported a small absolute survival benefit with PSA screening after nine years of follow-up. However, 48 additional patients would need to be diagnosed with prostate cancer to prevent one prostate cancer death. Although the report did not address quality of life outcomes, considerable data show the potential harms from aggressive treatments, including erectile dysfunction, urinary incontinence, and bowel problems.

Further sustaining the uncertainty surrounding screening, a report from the large United States trial, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, published concurrently with the European trial, found no benefit for annual PSA and digital rectal examination (DRE) screening after a seven to 10 year follow-up.

"Apart from issues of cost and acceptability, in order for prostate cancer screening to be valuable, it must reduce disease-specific morbidity and/or mortality," said Naidoo.

Harm from screening

- » Risks of biopsy: although early reports indicated that prostate biopsies very rarely (<1%) caused complications (e.g., bleeding, infection) serious enough to require hospitalisation, more recent studies suggest both higher rates of infectious complications and that the rate of infectious complications may be increasing over time. Hospitalisation rates for infectious complications in these studies have ranged from 0.6 to 4.1%.
- » Infectious complications can lead to sepsis, which can very rarely lead to death.
- » Prostate biopsy can also lead to anxiety and physical discomfort. Among 116 men undergoing biopsy in the Rotterdam screening study, 55% reported discomfort with the procedure, including 2% who had pain persisting longer than one week.
- » Being diagnosed with prostate cancer is psychologically distressing, but even patients with a negative biopsy result may be distressed. Chronic anxiety can follow a negative prostate biopsy because this apparently favorable result cannot completely rule out prostate cancer given the relatively high false-negative biopsy rate.

Overdiagnosis

"Overdiagnosis refers to the detection by screening of conditions that would not have become clinically significant. When screening finds cancer that would never have become clinically significant, patients are subject to the risks of screening, confirmatory diagnosis, and treatment, as well as suffering potential psychosocial harm from anxiety and labeling. Overdiagnosis is of particular concern because most men with screening-detected prostate cancers have early-stage disease and will be offered aggressive treatment," said Naidoo.

A number of reports have raised concerns about the risk of overdiagnosis with screening. While the



50-80%
of tumours involve
the prostate apex,
and around 85%
of patients have
multifocal disease
in the prostate.

lifetime risk of being diagnosed with prostate cancer has increased from one in 11 to one in six, the lifetime risk of dying from prostate cancer has remained around one in 34 following the advent of prostate-specific antigen (PSA) testing.

"Although approximately 80% of detected cancers are considered clinically important based on tumor size and grade, these are relatively crude prognostic markers. Autopsy series in men who died from other causes have shown a 30% to 45% prevalence of prostate cancer in men in their fifties and an 80% prevalence in men in their seventies," Naidoo said.

The risk of overdiagnosis of prostate cancer appears to increase with increasing age.

Risks of therapy

Even in the absence of treatment, many men found to have prostate cancer as a result of screening will have a lengthy period of time without clinical problems. However, undergoing radical prostatectomy and radiation therapies can lead to immediate complications:

- » The operative mortality rate ranges from approximately 0.1 to 0.5%, though the rate approaches 1% in men over 75 years.
- » Less serious, but more common complications include urinary incontinence, sexual dysfunction, and bowel problems. Radical prostatectomy can substantially decrease sexual function in 20% to 70% of men and lead to urinary problems in 15% to 50%.
- » External beam radiation therapy has been reported to cause erectile dysfunction in 20% to 45% of men with previously normal erectile function, urinary incontinence in two to 16% of previously continent men, and

bowel dysfunction in six to 25% of men with previously normal bowel function.

Approach to screening

"Although screening for prostate cancer with prostate-specific antigen (PSA) can reduce mortality from prostate cancer, the absolute risk reduction is very small. Given limitations in the design and reporting of the randomised trials, there remain important concerns about whether the benefits of screening outweigh the potential harms to quality of life, including the substantial risks for overdiagnosis and treatment complications," said Naidoo.

Men who are willing to accept a substantial risk of morbidity associated with treatment in return for a small reduction in mortality might reasonably choose to be screened. Men who are at increased risk of prostate cancer because of race or family history may be more likely to benefit from screening.

Recommendations

Because individual patient preferences for specific health outcomes are a deciding factor in determining whether to screen for prostate cancer, men who are potential candidates for screening should be engaged in discussions or decision-making processes that inform them and evoke these preferences:

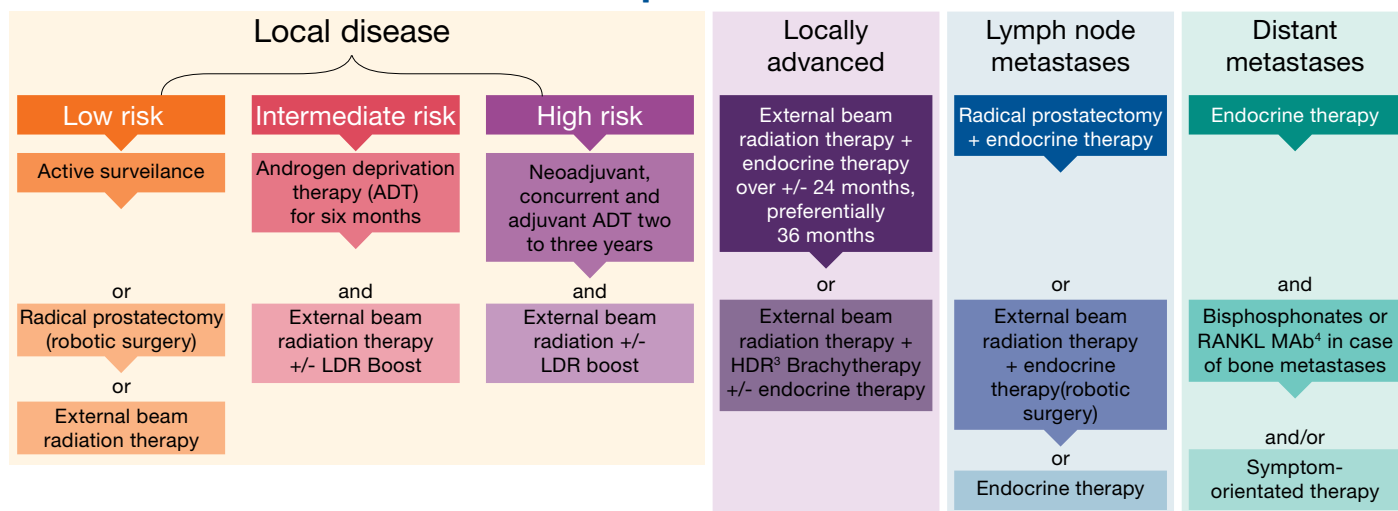
- » Discussions should present men with information on the risks and benefits of screening
- » Health care providers should periodically discuss prostate cancer screening with men who are expected to live at least 10 years and are old enough to be at significant risk for prostate cancer. We suggest that discussions begin at age 50 in average-risk men. In clinical practice

we suggest that discussions begin at age 40 to 45 in men at high risk for prostate cancer, including black men, men with a family history of prostate cancer, particularly in relatives younger than age 65, and men who are known or likely to have the BRCA1 or BRCA2 mutations.

- » Men who are at increased risk of prostate cancer because of race or family history may be more likely to benefit from screening, however there is relatively little evidence addressing this and these men should be informed that the potential benefits and risks of early screening are uncertain.
- » When a decision is made to screen, we suggest that screening be performed with PSA tests at intervals ranging from every two to four years. We suggest not performing digital rectal examination as part of screening.
- » When a decision is made to screen, we suggest that screening stop after age 69 or earlier when comorbidities limit life expectancy to less than 10 years, or the patient decides against further screening. Stopping screening at age 65 may be appropriate if the PSA level is less than 1.0 ng/mL.
- » Men with an abnormal DRE (if performed) or PSA level above 7 ng/mL should be referred, without further testing, to an interventional specialist who can evaluate them for a transrectal ultrasound-guided prostate biopsy.
- » We suggest that men with a PSA level between 4 ng/mL and 7 ng/mL undergo repeat testing several weeks later. Prior to repeat PSA testing, men should abstain from ejaculation and bike riding for at least 48



Treatment options available in SA



hours. Men with symptomatic prostatitis should be treated with antibiotics before retesting. Men with a repeat PSA level above 4 ng/mL should be referred for transrectal ultrasound-guided prostate biopsy.

Prognosis of a positive diagnosis

Risk Categories based on the biology of the disease – according to the National Comprehensive Cancer Network (NCCN):

- » Low risk: T1-2a, Gleason ≤ 6 and PSA < 10
 - » Intermediate Risk: T2b-T2c and/or Gleason 7 and/or PSA 10-20
 - » High: T3a or Gleason 8-10 or PSA >20 (very high T3b-T4).
- Cause Specific Survival (CSS) – the length of time from either the date of the diagnosis, or the start of treatment for the disease, to the date of death from the disease.
- » Low risk – five to 10 year CSS – >95%
 - » Intermediate risk – five to 10 year CSS – 75-90%
 - » High Risk – five to 10 year CSS – 60-80%.

Future prospects for treatment

a. Stereotactic Body Radio Therapy (SBRT) to the prostate gland

SBRT delivers fewer, high-dose fractions of radiation, providing a number of advantages, including a more convenient, shortened time course as well as a theoretical improvement in cancer response to larger daily radiation fractions. Early data from trials of SBRT show SBRT to be comparably effective in prostate cancer treatment.

b. Cryosurgery

Cryotherapy (also called cryosurgery or cryoablation) is the use of very cold temperatures to freeze and kill prostate cancer cells. With cryotherapy, an ultra-thin metal probe or needle is inserted into the prostate gland. This is done through an incision that lies between the anus and scrotum. To protect the urethra from the procedure's icy temperatures, a warm saline solution flows through a catheter.

The surgeon uses visual information produced by ultrasound as a guide during the process. A freezing liquid, such as liquid nitrogen or more commonly, argon gas, is infused through the probe into the prostate gland. The intense cold freezes the prostate and destroys any cancerous tissue it contains. Using the images from the ultrasound to identify the cancer tissue, the surgeon can limit damage to normal prostate tissue.

c. Genetic testing and treatment

Genomic testing is done on cancerous tissue taken from the prostate in order to provide information about how your prostate cancer might behave. By looking at the genetic makeup of the cancer, these tests may help predict whether your prostate cancer grows slowly or aggressively.

Genomic testing can be performed on both biopsy tissue and on tissue from an entire prostate following a prostatectomy. ^{SF}