The Epidemiology of Prostate Cancer and Trends in Victoria

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ABSTRACT

A majority of older men have detectable prostate cancer but only a small proportion will die from it. We cannot accurately distinguish cancers that require treatment from those that will grow slowly and not spread. Widespread prostate specific antigen (PSA) testing to detect prostate cancer early has caused a large increase in incidence but no commensurate fall in mortality. Reports of modest falls in mortality in some populations may reflect new treatments for advanced prostate cancer rather than an effect of PSA testing. Although PSA testing might have saved some lives, it might have affected the quality of many others.

BACKGROUND

Autopsy studies have shown that a majority of prostates, with advancing age, develop microscopic evidence of cancer that is often multi-focal. Prostate cancer tends to be biologically heterogeneous and commonly very slow growing. In an average lifetime, only a small proportion of these highly prevalent microscopic cancers grow sufficiently to threaten life; most men die with prostate cancer, not from it. Sadly, we do not know what causes this small proportion to grow and spread; neither can we accurately distinguish them from those that will remain indolent.

In short, we do not know what causes prostate cancer. Although epidemiological studies have given many leads, there are few established risk factors. After age, the strongest risk for prostate cancer is having a family history, especially if the relative was diagnosed at a young age. The importance of family history has led to a search for genes that may increase risk when mutated, but this search has not met with any success, probably as result of genetic heterogeneity.

Prostate cancer is androgen dependent, so variations in circulating hormones and in genes coding for hormones are current targets for research, as are variations in other genes coding for growth factors involved in normal prostate growth and development. Lifestyle factors such as drinking and smoking are not associated with risk, but some aspects of diet—saturated fat, antioxidant vitamins and phytoestrogens, for example—may play important roles and are being investigated, as are physical activity and obesity.

Localised prostate cancer is usually asymptomatic. With age, hormonal changes cause the prostate to grow and this growth (benign prostatic hypertrophy, or BPH) is contained within the gland’s tough outer capsule. Consequently, the urethra is compressed, causing the urinary problems commonly suffered by older men. In the absence of symptoms specific to cancer, most men used to be diagnosed either after the cancer had spread beyond the capsule or, incidentally, after surgical treatment of BPH (trans-urethral resection of the prostate, or TURP).

Since the discovery of the prostate specific antigen (PSA) in the mid-1980s, the diagnosis of prostate cancer has changed. PSA is a protease enzyme produced by the prostate that is elevated in the blood of men with established prostate cancer. It was first used to track the success of treatment, with falling PSA corresponding to response and rising PSA indicating treatment failure. With a blood test available, PSA testing was widely adopted for the early detection of prostate cancer. This has had a remarkable impact on incidence.

INCIDENCE TRENDS

In Victoria in 2000, 2548 men were diagnosed with prostate cancer, giving an age-standardised incidence rate of 72 per 100,000 men. Since 1989, prostate cancer has been the most commonly diagnosed cancer in men in Victoria. Figure 1 shows the age-adjusted incidence rate from 1982 to 1999. Prior to 1990, the rate was fairly stable; between 1990 and 1995, however, the annual incidence rate increased from 40 to 99 per 100,000.
has since declined to 72 per 100,000 in 2000.

Figure 2 gives incidence trends by broad age groups: less than 55 years old; 55–69 years old; and 70 years and older (note the logarithmic scale on the vertical axis that is required to visualise all trends at once). It appears that the strongest relative increase in incidence occurred in men aged less than 70 years old and that rates have risen most steeply in men aged less than 55 years old—a group in which prostate cancer has not commonly occurred in the past. Most of the impetus for early detection has been placed on men with life expectancies greater than 10 years.

Figure 3 illustrates the proportions of incident prostate cancers in 1990 and 2000, broken down by tumour differentiation/grade. There has been an enormous relative increase in moderately differentiated tumours and reductions in the proportion of well differentiated and poorly differentiated tumours. This change is consistent with an effect of early detection as a result of PSA testing.7

MORTALITY TRENDS

In Victoria in 2000, 693 deaths were attributed to prostate cancer and the age-standardised death rate was 16 per 100,000 men. The annual age-adjusted mortality rate increased slowly from 16 per 100,000 in 1982 to 20 per 100,000 in 1994 and 1995, but returned to 16 per 100,000 in 2000 (Figure 1). Figure 2 plots the age-specific trends in mortality rates alongside those for incidence, but there is only suggestive evidence of declining mortality and that is essentially restricted to men aged 55–69 years old.

Figure 4 displays age-standardised incidence rates for selected cancer registries for 1988–92.8 In this period, which included only the very early years of PSA testing, the highest rates in the world were observed in American black men (137), followed by American white men (100). The Victorian rate (48) was within the range of European countries (20–60). Overlaid on the incidence rates are the relevant mortality rates. Although there are marked differences in incidence between these populations, the mortality rates are very close.

DISCUSSION

Like many other populations, Victoria has experienced a dramatic increase in the diagnosis of prostate cancer, and the incidence rate now seems to be stabilising around twice its historical level. The widespread use of PSA blood tests, in the belief that early detection must be of benefit, has driven the increase in diagnosis. There is little evidence, however, that mortality rates in Victoria are falling as a result of this activity.
als are in progress to test this question, but their ability to give clear answers is being compromised by PSA testing available outside of the trial that is contaminating the control arm.9

Some populations report falls in prostate cancer mortality, but these falls cannot necessarily be attributed to PSA testing and may only retrace an increase in mortality that immediately preceded the testing.10 Potent anti-hormonal agents for the treatment of advanced prostate cancer became available around the same time as PSA testing, and the modest reductions observed in mortality could at least partly be attributed to them.11–13

Established programs for the early detection of cancers of the cervix, breast and bowel are founded on World Health Organisation criteria,14 which include the availability of not only a sensitive and specific test but also treatments of known efficacy for which known benefits outweigh any harm. The situation with prostate cancer does not fully meet these criteria and remains controversial, with strong advocates both for and against screening. It is probable, however, that some men’s lives have been saved as a result of PSA testing, early diagnosis and treatment with either radical surgery or radiotherapy. Many men, on the other hand, have undergone testing, been treated and unnecessarily suffered the side effects of treatment. This situation is unlikely to change until we have gained better knowledge of the biology of prostate cancer, which will lead to improved therapies and an enhanced ability to determine which cancers require treatment. Meanwhile, older men contemplating having a health check-up should seek to be informed about the pros, cons and possible consequences of PSA testing.

REFERENCES


