

Prostate cancer – is screening the solution?

Prostate cancer is the most common cancer in men in the UK, accounting for nearly a quarter of all new male cancer diagnoses and around 12% of all male cancer deaths.¹ Based on a similar time period, incidence rates in the USA are even higher at 56.9 per 100 000 men for all races and 234.6 per 100 000 for black men. One in 6 American men are at risk of being diagnosed with cancer of the prostate during their lifetime.²

An increased risk of cancer of the prostate is related primarily to age and family history and to a lesser extent to race. Prevalence is low under the age of 50 years and peaks at 50 - 80 years, while 5 - 10% of cases are thought to have a substantial inherited component, black men having an approximately trebled risk.² Prevalence rates have increased in recent times, partly due to increased case finding in asymptomatic men who are screened, and in tissue removed at transurethral prostatectomy for benign prostatic hypertrophy, where prostate cancer has been reported in up to 10% of cases.³

Cancer of the prostate is largely a disease of older men, and many cancers detected in asymptomatic patients will be indolent and slow-growing and will not shorten life. The average age of death from this disease in the UK is 80 - 84 years; by the age of 80 years, approximately 80% of men will have some cancer cells in their prostate. Many of these men will die from unrelated causes. Therefore, although 1 in 26 men (3.8%) in England and Wales will die from prostate cancer, many more will have low-risk indolent tumours and will die with, rather than from, the disease. By comparison, 1 in 2 men will die from cardiovascular disease and 1 in 53 from colon cancer.⁴

Cancer of the prostate is not a single disease entity, and its natural history is still not fully understood. It is rather a spectrum of diseases, ranging from indolent slow-growing tumours that may not cause any symptoms or shorten life, to aggressive rapidly growing tumours. However, some tumours change from being low-risk and slow-growing to high-risk aggressive tumours, and it is not possible to accurately predict which tumours will behave in such a manner.⁴ Therein lies the dilemma posed by screening programmes, which usually target older men (over the age of 50 years). Apart from uncertainties around the effectiveness of screening and a reported incidence of false-positive results of 10 - 15%⁵ – with the associated anxiety that this creates⁶ – many men will be at risk of undergoing aggressive surgical and irradiation therapy for a disease they may die with, rather than from. More recent access to less invasive brachytherapy may partially reduce this risk, but at what cost? It is almost inevitable that this less invasive treatment will also be over-used because of the same uncertainties that have influenced treatment choices until now, and the cost will undoubtedly limit access in the current funding environment.

It has recently been shown that with the type of cancer detected by screening an ageing population, 1 410 men will need to be screened and 48 treated for prostatic cancer to save one life, and a significant number of those may be left incontinent or impotent as a consequence.⁵ Does the benefit of screening for prostate cancer in an older population outweigh the risk? Overdiagnosis and overtreatment of prostatic malignancy, because of the absence of a good way of detecting which cancers will progress, arguably poses one of the major challenges of current clinical practice. Although the American health care model has advocated screening with digital rectal examination and prostatic specific antigen (PSA) since the early 1990s, there are still no specific guidelines in place in the UK, either for screening of high-risk families or of the general population, because of the above uncertainties.

Much hope was pinned on the completion of two recent landmark trials that studied the effect on mortality of screening for prostate

cancer, viz. the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the US-based Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.^{6,7} Both were extraordinary trials with an unprecedented magnitude of enrolled subjects, but failed to answer the critical questions. Both trials showed that the majority of cancers diagnosed were at stage 2, were nearly all adenocarcinomas, but there was little or no effect on mortality from the disease over a prolonged follow-up period. However, data from both trials support the notion that the benefits from screening may be restricted to younger age groups and that screening may be more important in these individuals.

Against this background, Heyns and colleagues report in this issue of the *SAMJ* their study on prostate cancer in younger men (under the age of 50 years). This is a retrospective review from an academic tertiary hospital, of a large number of patients without previous access to screening, who presented with prostate cancer, most being symptomatic at presentation. Notwithstanding the racial bias of this sample, which might have included relatively more high-risk patients than other reported studies, their data show quite convincingly that this age group included a significantly greater proportion of advanced high-grade tumours, with shorter survival than in older age groups. This finding lends some support to the notion espoused by the authors of the two recent international studies, that any mortality benefits to be achieved from screening are more likely to be achieved in younger patients, who would appear from this particular study to harbour higher-risk carcinomas that may benefit from earlier intervention. In reporting their experience, the authors have made a significant contribution to further understanding this disease in the South African context, and are to be commended.

Only 3% of the 1 571 patients reported by Heyns *et al.* were under the age of 50, and the low prevalence of prostatic carcinoma in this age group has implications when contemplating extending the age at which to commence screening. Restricting screening to individuals with risk factors such as positive family history in first-degree relatives may be a consideration. From an individual perspective, in a private health care setting, where individuals are fully informed of risks and benefits and funders willing to shoulder the increased cost burden, this policy could be considered. However, from the broader population perspective, and in the light of current uncertainties around the natural history of this disease, screening for prostatic carcinoma in any age group is unlikely to prove cost beneficial.

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