Time to reflect: helping patients to understand the natural history of prostate cancer

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No urologist doubts the efficacy and effectiveness of surgery in the management of urogenital cancer. At least 50% of patients with muscle-invasive bladder cancer (MIBC) will be cured after a radical cystectomy, with most recurrences occurring within 5 years of the initial treatment, and few urologists unhappy with discharging patients as cured after 10 years of follow-up.

Things are even better with renal cancer in all its variants. Approximately 70% of patients are cured, most recurrences occur within two years and many patients can, with confidence, be discharged after 5 years. There are well-documented late recurrences, up to 10 or more years after initial surgery, but these are rare and in no way justify all patients being followed up indefinitely. Even before 1978, when effective chemotherapy became available for testicular cancer, a combination of surgery and radiation therapy had pushed the five-year survival from just over 50% in the 1950s to 67% by the late 1960s.

We know from wider reading that effective interventions cause a significant fall in death rates from disease, most notably in cardiovascular disease. We also know what an effective screening programme delivers when we note the fall in both the incidence and death rate in cervical

The natural history of prostate cancer is different to other urological malignancies. The often extended survival should allow patients time to decide on the various options for management available to them. Peter Whelan suggests that healthcare professionals should not shoehorn prostate cancer into an inappropriate management paradigm and give patients the time they need to reflect at each step.

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cancer, the latter falling from over 3000 to 800 in the UK during the last 20 years.\(^2\)

Prostate cancer, the commonest malignancy we deal with, presents a whole different order of difficulties, not least the paradox that men, as a group, with the disease live longer than those without.\(^3\) However, ‘Get prostate cancer and live longer’ is not the sort of slogan that is likely to fill the coffers of prostate cancer charities; nor will it enable the obtaining of adequate funding to investigate this disease and diminish the still significant death rate it imposes.

At least 90% of patients are diagnosed with prostate cancer after testing for PSA and subsequently undergoing biopsy. A cursory glance at cancer information websites yields the fact that the 5- and 10-year survivals for low- and intermediate-risk patients is 100%. We know that since PSA testing became widespread in the early 1990s the length of the history of most prostate cancers has increased by 10 years. However, our approach and understanding of patients suggests that we are dealing with a disease with similar dynamics to other urogenital malignancies. Even attempts to form subcategories of risk – for example, age-related, comorbidity-related or family history – have not, seemingly, prevented patients believing that intervention equates with cure and non-intervention, under whatever guise it appears – watchful waiting, active monitoring, deferred treatment – is somehow second best.

LACK OF EVIDENCE

We are not helped in advising our patients by the paucity of level 1 evidence to guide them through these difficult choices, when so often few can get past the word ‘cancer’ and all it conjures. The fact that advice on treatment, both surgery and radiotherapy, is couched in terms of 10-year expected survival should tell patients that this is a slow-growing cancer in many cases. But this does not impact on patients and their relatives, not least in the NHS system where arbitrary targets on diagnoses and treatment are imposed, reducing all cancers to being the same.

There is no level 1 evidence for radiation therapy, external beam therapy or brachytherapy, let alone the more experimental treatments of cryotherapy or focal therapy.\(^4\) There are two randomised trials of surgery against observation: the US PIVOT study showed no difference, while the Scandinavian study showed a modest benefit for surgery.\(^5\) In the Scandinavian study, a total of 695 men were randomised between 1989 and 1999. In 2014, 200/347 men in the surgery group had died with 63 deaths attributed to prostate cancer, while 247/348 had died in the watchful waiting group with 99 attributed to prostate cancer. The absolute benefit was 11%, meaning eight needed to be treated for one to benefit. Put more aggressively, 7/8 derived no benefit from the surgery, which is a very long way from outcomes in other cancers we treat. The most important result from this study is that 137 men in the surgery group and 148 from the watchful waiting group died from something else.

The 10-year results from the UK ProTech study is due to be published this year. This, will, for the first time, provide randomised data on radiation therapy – but we can already guess that 10 years may be too early to give a satisfactory, let alone a definitive answer.

Death rates have also shown little more than a modest benefit to intervention. There were 31 000 deaths attributed to prostate cancer from 100 000 incident cases in the USA in 1980, whilst there were 29 792 deaths in 2014 on just over 240 000 incident cases.\(^6\) A paper by Konety et al. has shown that most post mortem cases found in earlier eras are now being found, especially in the USA, by PSA testing and, by definition, we have known since the 1950s that these cases are indolent.\(^7\) These cancers didn’t trouble men when we didn’t know they were there, so won’t do now just because we find them.

To add to our problems, high-risk patients have only been accepted for surgery in the last decade, so most of our outcome information for this group is based on radiation therapy groups. Because the dosage of radiation has increased markedly in recent years, we do not have long-term data, even from observational studies, to know what improvement this brought to survival.

Finally, recent work has shown that our ability to estimate the life expectancy of patients in general is poorly developed.\(^8\) Albertsen makes a reasonable criticism of the PIVOT trial in noting that too many patients died before the benefits of surgery could be assessed, although these went into the trial with a notional life expectancy of greater than 10 years, thus emphasising our lack of skills in this area.\(^9\)

HOW DO WE HELP PATIENTS?

How can we reconcile these difficulties and enable our patients to access the best current management for them as an individual? Not, I would suggest, by handing out three separate leaflets to patients and asking them to come to the next clinic and say what they want to do. We need to establish their understanding of the length of the disease in its untreated state so that they know urgent decisions are not called for. They need to know that only with incipient cord compression or painful metastases is urgent treatment essential. Very few patients will ever have these problems.

Next, we need to assess their life expectancy as best we can. A recent study showed that nearly half of patients going into a prostate cancer trial were on four or more drugs for other conditions, which is a reasonable predictor of significant morbidity.\(^1\) What little evidence we have indicates that general physicians are best
Deferring treatment in order to maintain an active sex life may be worth a discussion with some patients. Most prostate cancer patients will have enough time to consider the options.© Mark Clarke/Science Photo Library)

must be empowered with the knowledge that they can do this safely – and their relatives must understand this equally well.

Virtually all prostate cancer occurs in the last quarter of a man’s life. At this stage, their hopes, goals and expectations will be different to those of younger men with perhaps half their lives in front of them. We are gaining information, even if serendipitously, in cohort and observational studies of surgery in high-risk or locally advanced disease, and patients coming out of active monitoring studies to receive treatment. Whilst no substitute for randomised controlled trials, observational and cohort studies, these patients, who in many cases are likely to fail biochemically early, may help us decide whether deferring treatment in order to preserve an active sex life is a discussion worth having with the patient.

CONCLUSION

As a result of the tools we have been handed – primarily PSA early diagnosis – we have tried to shoehorn prostate cancer management into an existing paradigm which has proven successful for other urological malignancies. The data we have do not show equivalence and treatment for patients coming out of active monitoring needs to be imparted, as patients will live with these effects for a long time. We also need much more information on the possible psychological effects of not treating a cancer and whether understanding the longevity of the disease mitigates this.

At each phase of prostate cancer – initial diagnosis, rising PSA, loco-regional spread, asymptomatic metastases, hormone unresponsiveness – the patient must have the opportunity to pause and reflect, weighing up the advantages of a particular course of action, as there is no evidence to support immediate therapy other than seeing the PSA fall. At the same time, they

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REFERENCES.