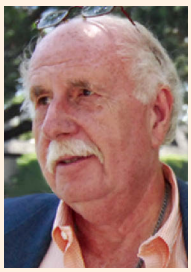
Thoughts on the Role of Active Surveillance for Prostate Cancer



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Albeit with a lifetime risk of death from prostate cancer of just 3%, this disease represents one of the most challenging issues facing physicians and men today, especially with an ageing population and a dramatic 2-fold increase in risk being associated with prostate-specific antigen (PSA) screening. The situation is one of the worst shortcomings of the healthcare system notably in the USA.

The clinical assumption over the past 20 years that the PSA test should be innately beneficial, based on the fair concept – as with other malignancies – that earlier diagnosis can raise the level of cure, has proved incorrect. The consequence is overdiagnosis and overtreatment, with attendant life-altering morbidities, including sexual, urinary and bowel dysfunction, and which has not significantly improved life- expectancy in over one million men in the US alone [1].

A major dilemma in the detection and treatment of prostate cancer is it displays extraordinary heterogeneity, ranging from slow growing, non-aggressive, non-life threatening tumours in most cases to aggressive life-threatening metastatic tumours in others. This is exemplified by the major discrepancy between its observed clinical prevalence and its high prevalence at autopsy. Therefore, with the now questionable necessity for population screening, there is clearly a need for other options regarding diagnosis and treatment. A randomised clinical trial (PIVOT) of prostate cancer patients with localised ('low-risk') disease treated by radical prostatectomy vs simple 'wait and see' showed no benefit of the former among subjects with PSA ≤10ng/ml [2]. The caveat here is that avoidance of overtreatment of 'low-risk' prostate cancer is critically important because the benefits are becoming increasingly questionable. However, there has been a slight decline in all-cause mortality in men with PSA levels >10ng/ml, and potentially a benefit for men with intermediate- to high-risk prostate cancer [2].

These findings might encourage ongoing efforts to minimise the harm of overdiagnosis and overtreatment by: i) stratifying prostate cancer patients into low-, intermediate- and high-risk groups, and ii) adopting more frequently the strategy of 'active surveillance' (AS) for low-risk patients (Gleason ≤6, PSA ≤10ng/ml* and clinical stage T1c–T2a) vs. immediate treatment. As the result of the consensus of an independent panel at a State-of-the-Science Conference on the role of AS in the management of localised prostate cancer convened by the NIH, it was stated that "AS has emerged as a viable option that should be offered to patients" [3] (In the UK, this strategy is adopted for men with <6 Gleason status who are >70 years of age). The panel also "suggested consideration should be given to removing the anxiety-provoking term 'cancer' for this condition" [3; and see below[.

[*My concern is that, unless you know the patient's PSA, you cannot include it as a criterion for stratifying risk. However, no absolute level of PSA seems to suffice, e.g., some patients with cancer have a PSA of 0.5ng/ml whereas others with a PSA of 11ng/ml do not. Therefore, you have to return to population screening of symptomatic men, which has contributed to the necessity for AS.]

AS patients need to be re-examined and re-biopsied as and when necessary. Aggressive treatment is offered only for signs of clinical progression, although criteria for defining progression remain controversial and/or are in need of refinement. Ridout et al. [4] discuss this matter in "New Approaches in Active Surveillance for Prostate Cancer" in this issue (pps. 185-187), with a focus on an interesting incorporation of magnetic resonance imaging into the assessment of prospective candidates for AS. In addition to their endeavours, studies designed through the Prostate Active Surveillance Study (PASS [5]), may help to identify and validate biomarkers differentiating non-aggressive from aggressive prostate cancers. Such information should improve decision-making on patient criteria for inclusion, as well as monitoring, strategies.

Last, but not least, although AS remains under utilised in the US [3] despite increasing knowledge of overdiagnosis and overtreatment, the harms thereof, and the awareness of the option of AS for prostate cancer, I do believe a major factor lies in using the word 'cancer'. Perhaps, with few more feared words in any language, 'cancer' is undoubtedly emotionally charged. Once a patient hears the word, the immediate instinct is "cut it out" or "get rid of it", otherwise any subsequent discussion becomes difficult, if not impossible. Once diagnosed, the time around reaching a decision to proceed with conventional treatment or AS is going to cause considerable distress, according to Ridout et al. [4] and others. A major concern is that, while under AS is taking place, will a cancer that might initially have been treated and 'cured' progress beyond the prostate to a state that is incurable? This thinking may prompt patients/oncologists to take unnecessary and precipitous action. For this reason, it has been suggested, initially by Oppenheimer [6], and recently by the NIH-convened Panel on the role of AS in the management of localised prostate cancer [3], that a term other than 'cancer' be used. This is worthy of further discussion, but is beyond our limitation here. As Welch et al. [7] noted "the cellular abnormality that pathologists call prostate cancer is far too prevalent to be consistently clinically important" [7]. This must be recognised as of importance to future thoughts on adopting the AS strategy. ■

References

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