PSADT of metastasis-free survival than those with a PSADT of 1 year. A subsequent update by Freedland et al. [7] stratified patients’ prostate cancer-specific survival based on PSADT (≤3, 3–8.9, 9–14.9, ≥15 months), with those with a PSADT of ≤3 months having the highest risk of prostate cancer-specific mortality (PCSM). Similar results after definitive external beam radiotherapy were reported by Zhou et al. [8], who showed that a PSADT of <3 months was associated with a 5-year PCSM of 15%, vs 4% in those men with a PSADT of ≥3 months. An extremely short PSADT (i.e. <3 months) has also been associated with worse overall mortality after radical prostatectomy or radiation therapy [3]. Specifically, in one study the median overall survival for patients with a PSADT of <3 months was ≈6 years, whether they had surgery or radiation. This has led some investigators to consider a PSADT of <3 months as a potential surrogate endpoint for PCSM.

The converse correlation of a long PSADT with relatively low rates of metastases has led to the integration of PSADT with other factors (i.e. Gleason score, surgical margin status, absolute PSA value) to optimize the selection of patients for salvage radiotherapy after postoperative biochemical failure. A retrospective multi-institutional analysis by Stephenson et al. [9] showed that patients with Gleason scores of 4–7, a PSA level of ≤2 ng/mL before radiotherapy, positive surgical margins, and a PSADT of >10 months had a 4-year progression-free probability of 77% after salvage radiotherapy, compared to only 12% in those patients with Gleason scores of 8–10 and a PSA level before radiotherapy of >2 ng/mL.

One of the most common methods to calculate PSADT assumes an exponential rise in PSA and first-order kinetics. PSADT would then be calculated by taking the natural logarithm of 2 divided by the slope obtained from fitting a linear regression of the natural log of PSA on time. An appropriate starting point and a sufficient number of values should be used to make this estimate. A recent National Cancer Institute working group meeting on PSADT in 2006 recommended using a minimum starting PSA level of ≥0.2 ng/mL to diminish the potential bias from using a lower starting value. Furthermore, a minimum of three PSA values each separated by at least 4 weeks was recommended to improve the representation of the PSADT calculation. Once a PSA failure has been established, all PSA values should be used regardless of whether they are consecutively increasing, and ideally should include all values over a period of 12 months to reflect the patient’s current disease activity.

Other recommendations from this working group included using the same PSA assay at the same laboratory whenever possible, and to draw the serum at the same time of day. The PSA values included in the calculation are recent (≤10 months; see PSADT section).
should also be obtained in a relatively stable testosterone state (e.g. normal testosterone or castrate) and not during a recovery period after hormonal therapy. The presence of other factors that might cause nonmalignant PSA increases needs to be considered, e.g. recent sexual activity, perineal, rectal or urethral manipulation. After radiotherapy (especially brachytherapy implants), the possibility of a benign PSA 'bounce' should be considered before assuming a definitive biochemical failure and subsequent calculation of PSADT.

CONCLUSION

Regardless of the definition of failure used, or the method by which PSADT is calculated, PSADT has been shown to be significantly associated with the time to metastases and cancer-specific death. The optimum thresholds for PSADT for clinical decision-making continue to be investigated, and a single threshold is unlikely for all cases. However, the currently available data suggest that PSADT is most useful at the ends of the spectrum. An extremely short PSADT after therapy (e.g. <3 months) is associated with significantly worse clinical outcomes, whereas patients with a relatively long PSADT (e.g. >15 months) are unlikely to die from their disease. While PSADT is a significant predictor of outcomes, it should be incorporated with other important clinical and pathological factors, e.g. the Gleason score, to optimally assess the prognosis for the individual patient.

CONFLICT OF INTEREST

None declared.

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Abbreviations: PSADT, PSA doubling time; PCSM, prostate cancer-specific mortality.

‘TIME, GENTLEMEN, PLEASE’ FOR WATCHFUL WAITING IN PROSTATE CANCER? Laura M. Kenny, Sarah Ngan and Jonathan Waxman – Department of Oncology, Imperial College London, London, UK

Accepted for publication 18 April 2007

INTRODUCTION

There is a certain view of prostate cancer as a condition with which some patients live sibiotically, a condition that might never cause symptoms nor affect life-span. This view was formed based on inferential evidence from the Veterans’ 1967 studies [1], which suggested that the early treatment of advanced prostate cancer was not thought to have a survival advantage. For a condition that is so prevalent, it is surprising to note the fragility of the evidence base that supports passive management. In the classic Veterans’ studies patients with advanced prostate cancer were randomized to placebo or hormonal therapy. Survival was similar in both groups, but for those patients treated with diethylstilboestrol, mortality rates from oestrogenic toxicity affected overall survival [1]. In Volume One of the ‘Apochrypha of Prostate Cancer’ it is written...