

Active surveillance for low-risk prostate cancer; a plea for increased urologist awareness

Abbreviations: PSA, prostate specific antigen; AS, active surveillance; MUSIC, michigan urological surgery improvement collaborative; RP, radical prostatectomy

Editorial

Prostate cancer is the most commonly diagnosed malignancy in men as 1 out of 6 men are at risk for being diagnosed with this disease during their lifetime. The observed increase in the prevalence of prostate cancer has been mainly attributed to the widespread use of prostate specific antigen (PSA) testing for opportunistic screening.¹ Screen-detected prostate cancer nowadays accounts for approximately 50% of newly diagnosed cases; moreover most of these patients are diagnosed with favorable risk Ca P; (i.e.T1c-T2a, Gleason Score ≤ 6 , PSA<10).

The diagnosis of screen detected favorable risk prostate cancer, which potentially would have never caused symptoms or become a clinical problem during the individual's life time constitutes "over diagnosis" Moreover, it is well-known that over diagnosis goes hand-in-hand with overtreatment, as more than 80% of newly diagnosed favorable risk prostate cancers will go on to receive active treatment. However, such unnecessary interventions could potentially be spared and treatment side effects, along with their negative impact on quality of life, could be avoided.²

In efforts to protect men diagnosed with insignificant prostate cancer from the harms of overtreatment, active surveillance (AS) has emerged as an alternative management strategy and is applicable for the wide proportion of men diagnosed with low-risk prostate cancer. AS is based on the idea that the lead-time from diagnosis to clinical progression is usually long for low-risk disease, and at the first signs of higher-risk disease, treatment can be implemented and the cancer can be treated within the opportunity of cure. It is a strategy to defer (sometimes indefinitely) radical treatment (radical prostatectomy or radiotherapy) in men with curable, low risk prostate cancer, aiming at avoiding treatment for those who do not actually need it. The potential benefit is that the side effects of treatments (sexual dysfunction, continence) can be postponed or avoided, with little to no impact on future cure rates, and for lower treatment costs.

Although at least half of newly diagnosed prostate cancer patients have favorable prognostic factors (PSA ≤ 10 ng/ml, stage T1c or T2a, Gleason score 6 in 2-3 cores) and should theoretically be candidates for AS, only $\leq 20\%$ of eligible patients actually are reported to go down this path. We, as urologists, should be held responsible for this discrepancy at least to a degree, as patients are usually under-informed about A.S. On the contrary, patients are sometimes persuaded to receive active treatment. The overwhelming 49% rate of AS for men diagnosed with early stage disease reported from the state of Michigan after the establishment of the Michigan Urological Surgery Improvement Collaborative (MUSIC) is clear evidence of the urologist's vital role in the acceptance of AS.³ Michigan urologists

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agreed to set a goal of measuring surveillance rates and that was enough to raise the AS rate to nearly half of all eligible patients.

If a patient has been offered AS and a shared decision has been reached between the patient and the urologist to proceed with this strategy, a confirmatory biopsy should be performed within the first year. The reason is that staging errors are common when one relies on a single 12-core TRUS-guided biopsy. These confirmatory biopsies can be performed by the transrectal or perineal route and should also include sampling of the anterior and anterolateral horn of the prostate. Transperineal template biopsies may be more accurate in determining the final Gleason score and risk category according to some authors, however with an increased risk of urinary retention.⁴ The number of cores taken at a confirmatory biopsy is also a matter of debate, although evidence exists that there is no difference in detection between 24 cores versus more (median 62).⁵ Recently, there is increasing evidence that MRI-TRUS fusion biopsies may be the optimal route of biopsy in this clinical scenario. The results of confirmatory biopsies are vital as studies have shown that up to 35% of men may no longer be candidates for AS.⁶ Once the confirmatory biopsy result is compatible with pursuing AS, further repeat biopsies are required to be performed every 2-3years, based on the A.S protocol.

While within an A.S protocol while on an AS protocol, nearly 1 out of 3 patients will be re-classified or re-staged as high risk for disease progression and will be offered curative treatment. Upgrading on repeat biopsy, namely a higher Gleason score, is the most common reason for transition to treatment, followed by patient or physician anxiety or fear of untreated cancer. Regarding patient safety while on AS, evidence suggests that deferring treatment does not adversely impact on the oncological outcome as compared to immediate treatment. Studies comparing immediate radical prostatectomy (RP) versus delayed RP when AS fails established no differences between biochemical recurrence rate, positive surgical margins, extra prostatic extension, continence status and risk of advanced or incurable cancer.^{7,8} Based on maturing cancer specific mortality under A.S is very low, although not zero.⁹ In a recent review Klotz reported a 1-5% cancer specific mortality at 15years for the low risk group.¹⁰

In the future, multi parametric MRI and molecular tests will definitely play a major and growing role in patient selection and, follow-up. It appears likely that MRI will decrease the number of biopsies on follow-up or might even replace them at least to a degree. Urologists, our role is adequately inform, discuss and offer A.S to patients who are eligible and willing to commit to this management strategy. Published evidence would suggest that we can and should do better in embracing active surveillance. Let's not forget our first commandment as a physician: primum nil nocere.

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Conflict of interest

The author declares no conflict of interest.

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