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PROSTATE CANCER

Optimizing active surveillance: patient and protocol

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Active surveillance (AS) is recommended for the management of low-risk prostate cancer, aiming to minimize overtreatment whilst identifying those men whose cancer has progressed to require treatment. However, protocols vary, and there is no standard set of monitoring parameters.

In a recent study, Kates and colleagues compared indications for intervention in two widely used protocols—the Prostate Cancer Research International Active Surveillance (PRIAS) programme and the Johns Hopkins Hospital (JHH) protocol, which vary in their monitoring parameters, with JHH using annual prostate biopsy and PRIAS using a combination of biopsy at 1, 4 and 7 years plus PSA kinetics to trigger intervention. Kates *et al.* retrospectively reviewed men on the JHH programme to examine whether they would have been managed differently on PRIAS. The PRIAS protocol would have spared men the discomfort and potential adverse effects of annual biopsies while still resulting in reclassification requiring treatment in a reasonably timely manner. However, nearly one-sixth of men would experience a 2-year delay in reclassification, which could affect cancer-specific mortality. The use of PSA kinetics identified high-risk disease in 11% of men nearly 5 years before biopsy would have reclassified them. However, 12% of men who would have been treated under this protocol would never have received treatment had they been monitored by JHH, suggesting that overtreatment could be a concern for men enrolled on PRIAS.

Several questions arise from the study, all of which require further investigation; namely, should men undergo annual biopsy to prevent a delay in reclassification in only one in six, and is this delay clinically significant? Should we be using PSA kinetics to prompt treatment earlier in 11% of men if it means overtreating a similar proportion? Potential answers must take into account not only the clinical outcomes, but also the effect on the patient, the additional burden on urologists, and the economic impact.

In a second study to investigate optimizing AS, Ha *et al.* examined the effect of using PSA density (PSAD) in AS protocols. Programmes vary in their inclusion of this parameter—the National Comprehensive Cancer Network (NCCN) programme uses a PSAD cut-off value of <0.15 ng/ml, whilst PRIAS uses a threshold of 0.2 ng/ml and the UCSF criteria do not include PSAD at all. Ha *et al.* showed that removing PSAD from the NCCN and PRIAS programmes expanded eligibility, but also increased the frequency of upgrading or upstaging at prostatectomy. Adding PSAD to the UCSF criteria and reducing the PRIAS threshold to 0.15 ng/ml reduced the frequency of upstaging, but >30% of patients still experienced upgrading/upstaging with all three criteria using the lower PSAD cut-off. The authors suggested reducing this value even further to 0.085 ng/ml, which would reduce upgrading, but exclude up to 60% of men from AS programmes.

AS is undoubtably a reasonable management strategy for low-risk prostate cancer. However, controversy regarding the optimization of protocols for the majority of patients looks set to continue.

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Original articles Kates, M. *et al*. Indications for intervention during active surveillance of prostate cancer: a comparison of the Johns Hopkins and PRIAS protocols. *BJU Int.* doi:10.1111/bju.12828 | Ha, Y.-S. *et al.* Prostate-specific antigen density toward a better cutoff to identify better candidates for active surveillance. *J. Urol.* doi:10.1016/j.urology.2014.02.038