Reasons for Abandonment of Active Surveillance in Men with Prostate Cancer

Active surveillance (AS) of prostate cancer allows many men to delay or avoid prostate directed therapy for clinically low risk disease. This is an accepted treatment option with increased use worldwide. Inherent to AS and in contradistinction to watchful waiting is that this approach involves actively monitoring patients for early signs of progression or changes in risk profile that may lead to adverse oncologic outcomes if the primary tumor remains untreated. At this point, abandonment of AS for potentially curative prostate directed treatment is recommended.

The rate of abandonment of AS for treatment has been reported in multiple series and depending on follow-up length is not negligible. Two well described, single institution experiences with AS report treatment rates of 45% and 57% at 15 years.1,2 Outside of institutions with extensive experience with AS, outcomes are not as well-known and likely differ.

In a cohort of Swedish men identified through the Göteborg arm of the European Randomized Study of Screening for Prostate Cancer and managed with AS, the 10-year and 15-year treatment-free survival was substantially lower at 47% and 34%, respectively.3 The PASS (Prostate cancer Active Surveillance Study) is a prospective multicenter AS study sponsored by the Canary Foundation and in this trial 19% of men were treated after a median follow-up of 28 months.4 Patient selection criteria, monitoring strategies and triggers for further intervention differ between these groups, which will affect rates. However, the majority of men who receive deferred treatment do so for some change in clinical status. Abandoning surveillance does not indicate failure with this approach. Rather it reflects successful disease monitoring and timely, more appropriate treatment. As most disease reclassification occurs as a result of changes in tumor histology, careful AS requires close monitoring with repeat prostate biopsies over time.

Other than for disease reclassification, how often and for what reasons do men abandon AS for prostate cancer? Again, depending on the practice setting, these rates and reasons will vary. In the study by Berger et al 9% of men left for nonclinical reasons including feelings of uncertainty and fear of cancer.5 Even within the confines of a clinical trial such as the PASS or the PRIAS Project (Prostate cancer Research International Active Surveillance), 6% to 14% of participants discontinued AS for reasons other than clinical progression.4,6 Anxiety is a common emotion after any cancer diagnosis and is potentially more pronounced when curative therapy is not recommended. Although some earlier studies suggest that anxiety is associated with shorter time to treatment on AS, recent reports describe relatively low anxiety levels for men while on AS at around 15% and that anxiety actually decreases with time.7–9 More specifically investigators found that intolerance of uncertainty and moderate to severe urinary symptoms appear to contribute to anxiety while on AS and, therefore, efforts to control or reduce these may be helpful.9,10 Furthermore, refusal to adhere to surveillance testing may drive some men toward other interventions.

In this issue of The Journal (page 000) Kelly et al studied nonclinical predictors of abandoning surveillance for men cared for under a large health maintenance organization.11 After a median follow-up of 2.9 years 27% of men underwent treatment after a period of AS, a rate consistent with other series. Nonclinical factors such as race and education had a small association with treatment. African-American men were marginally more likely to be treated than Caucasian men as well as men living in lower education areas. These differences did not remain for the fraction of men who adhered to a defined AS protocol with repeat testing for signs of clinical risk re-stratification. Changes in Gleason grade and prostate specific antigen doubling time less than 48 months were most strongly associated with treatment for the entire cohort, yet while nearly all men (96.5%) received at least 1 surveillance prostate specific antigen test only 53% underwent repeat biopsies. These data raise the question of how much patient monitoring actually occurs after starting AS outside of a clinical trial or experienced institution.
Also in this issue Loeb et al (page 000) used the SEER (Surveillance, Epidemiology, and End Results)-Medicare data set to evaluate the intensity of monitoring of men on expectant management.12 With the inherent limitations of identifying true active surveillance cases in a large data registry, disease monitoring was abysmal, with fewer than 13% of men having a prostate biopsy beyond 2 years. Only 5% and 11% of men met the surveillance strategies set forth in the University of Toronto and Johns Hopkins experiences, respectively.

The reasons for poor adherence are unknown. However, a lack of clear guidelines, inadequate clinician experience and patient reluctance to undergo repeat testing may be implicated. These findings call into question the safety of this approach on a larger scale and may represent barriers to wider adoption. AS is predicated upon identifying early signs of progression when further therapy can be administered. However, without close monitoring, the window of curability may be missed.

Until recently there have been no concise guidelines on how to perform AS. The National Comprehensive Cancer Network® and European Association of Urology have now published guidelines including patient selection and monitoring strategies. Cancer Care Ontario has also published a set of guidelines for AS that were recently endorsed by the American Society of Clinical Oncology. These guidelines may help clinicians and patients adhere to a set of expert standards for prostate cancer monitoring and perhaps improve compliance with surveillance testing. They may further alleviate uncertainty by applying clear definitions of risk reclassification or triggers for further intervention.

Novel technologies and disease registries may also help standardize care and provide resources to facilitate disease monitoring. Patients should be made aware up front that there is a reasonable likelihood that other treatments may be recommended at some point for their prostate cancer and that until further studies clarify the roles of multiparametric magnetic resonance imaging and novel biomarkers for use in AS, repeat prostate biopsies are critical.

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REFERENCES


