News and Views From the Literature

Heterogeneity in Active Surveillance Protocols Worldwide

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Prostate cancer screening is controversial due to downstream consequences that include overdiagnosis and overtreatment of low-risk tumors. In the 2014 National Comprehensive Cancer Network Guidelines, active surveillance is recommended as a management strategy to avoid the side effects associated with definitive therapy that may be unnecessary.[1] Although the use of active surveillance has recently increased in many parts of the world,[2] there is no consensus on patient selection and follow-up protocols.[3] Two recent studies performed surveys of practicing urologists to characterize the heterogeneity in the type, frequency, and sequence of follow-up testing used in active surveillance.

Active Surveillance for Low-Risk Prostate Cancer: Knowledge, Acceptance and Practice Among Urologists

Gorin MA, Eldefrawy A, Ekwenna O, et al.

Prostate Cancer Prostatic Dis. 2012;15:177-181

Surveys were emailed to 4987 urologists to examine current practice patterns regarding active surveillance. These urologists were identified through the directory for the American Urological Association and other online resources. A total of 425 (9%) urologists responded to the survey, of which 387 (91%) were familiar with active surveillance and formed the study population. Most of the respondents were from the United States (69%), 51% practice at least partly in a university setting, and 44% were fellowship trained.

Overall, 95% of these urologists reported that they manage patients with active surveillance. For eligibility criteria, 94% and 74% of respondents agreed on serum prostate-specific antigen (PSA) levels < 10 ng/mL and a Gleason score $\leq 3 + 3 = 6$, respectively. However, there was wide variability in the age range, maximum

number of positive cores, and volume positive for tumor that was considered acceptable for active surveillance.

There was also significant heterogeneity in the follow-up protocols. A total of 24% felt that magnetic resonance imaging (MRI) had a role in following patients. In terms of timing for a second prostate biopsy for men enrolled in surveillance, 58% felt that it should be performed at 12 months, 30% recommended earlier repeat biopsy, and 12% typically waited until 15 to 26 months to perform another biopsy.

There was also no consensus on the optimal time interval for subsequent repeat biopsies, with 52% recommending this within 12 months, 12% repeating the biopsy 15 to 18 months later, 30% at 24 months, and 6% at 36 months.

Finally, in the minority of respondents who reported that they do not use active surveillance, the main reasons were fear of missing the opportunity for cure and fear of undergrading on biopsy. A smaller proportion also cited legal liability as a concern.

Active Surveillance for Low-Risk Prostate Cancer: Diversity of Practice Across Europe

Azmi A, Dillon RA, Borghesi S, et al.

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Surveys on active surveillance practices were sent to 2959 practicing urologists in European Union countries in three phases from 2009 to 2011, yielding a total of 226 (8%) responses. Overall, 97% reported that they offer active surveillance to patients. Of these, 53% only perform active surveillance as part of a clinical trial or protocol, whereas the remaining 47% offer active surveillance outside of any set protocol. This allowed the authors to perform several comparisons of active surveillance practices between these groups.

For patient selection, 51% reported using different criteria for older and younger patients. There was majority consensus that candidates should have a serum PSA level ≤ 10 and a Gleason score $\leq 3 + 3 = 6$ to be considered for active surveillance (86% and 87%, respectively). However, a significantly higher proportion of respondents performing surveillance as part of a trial or protocol used PSA and Gleason criteria for selection, compared with those not participating in a clinical trial or set protocol. There was less agreement about specific restrictions for selection on the basis of age, clinical stage, and biopsy core data.

For men who initiate surveillance, 96% of urologist respondents perform a digital rectal examination (DRE) at baseline and 70% check the free to total PSA ratio. MRI was significantly more likely to be used among those participating in a trial/protocol (35% vs. 21%, $P = 0.039$), and bone scans were used by 25%.

During follow-up, 100% of urologists indicated that they used PSA to monitor patients, followed in descending order by DRE (89%), prostate biopsy (83%), and MRI (8%). Although 77% of urologists perform a follow-up biopsy within the first year, only 18% of urologists recommend serial biopsies annually. Fifteen percent perform rebiopsy only once during follow-up, and 5% only perform repeat biopsy if prompted by a rising PSA or change in DRE. Finally, the most common triggers for intervention were Gleason grade progression (87%) followed by PSA doubling time ≤ 3 years (60%) and DRE (56%).

A limitation of both studies is the exceptionally low response rate, raising concerns about the validity and generalizability of these results, or whether there are systematic differences between respondents and nonrespondents. In addition, neither study evaluated the use of new markers such as PCA3[4,5] and the prostate health index,[6,7] which have recently become available and have been studied in active surveillance populations.

Nevertheless, these studies show that among some practicing urologists across the United States and European Union, there is considerable heterogeneity in the type, frequency, and sequence of testing used during active surveillance. These studies highlight the importance of further investigation into the comparative effectiveness of different protocols for active surveillance. ■

References

1. National Comprehensive Cancer Network 2014 Clinical Practice Guidelines: Prostate Cancer. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed June 13, 2014.
2. Loeb S, Berglund A, Stattin P. Population based study of use and determinants of active surveillance and watchful waiting for low and intermediate risk prostate cancer. *J Urol*. 2013;190:1742-1749.
3. Ganz PA, Barry JM, Burke W, et al. National Institutes of Health State-of-the-Science Conference: role of active surveillance in the management of men with localized prostate cancer. *Ann Intern Med*. 2012;156:591-595.
4. Tosoian JJ, Loeb S, Kettermann A, et al. Accuracy of PCA3 measurement in predicting short-term biopsy progression in an active surveillance program. *J Urol*. 2010;183:534-538.
5. Lin DW, Newcomb LF, Brown EC, et al. Urinary TMPRSS2:ERG and PCA3 in an active surveillance cohort: results from a baseline analysis in the Canary Prostate Active Surveillance Study. *Clin Cancer Res*. 2013;19:2442-2450.
6. Tosoian JJ, Loeb S, Feng Z, et al. Association of [-2]proPSA with biopsy reclassification during active surveillance for prostate cancer. *J Urol*. 2012;188:1131-1136.
7. Hirama H, Sugimoto M, Ito K, et al. The impact of baseline [-2]proPSA-related indices on the prediction of pathological reclassification at 1 year during active surveillance for low-risk prostate cancer: the Japanese multicenter study cohort. *J Cancer Res Clin Oncol*. 2014;140:257-263.