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EDITORIAL COMMENT

Active surveillance (AS) has been widely accepted as a first-line management approach in men with low-risk prostate cancer. While AS provides an avenue to reduce risk of overtreatment without compromising oncological safety, there remains a lack of consensus on the optimal approach to monitoring. An ideal surveillance strategy would be one that minimizes invasive testing such as prostate biopsy without conceding adverse oncologic outcomes. Thus, several studies have sought to identify men at higher risk of reclassification so as to more carefully select when biopsy is truly necessary.

In the current study, the authors explored predictors of reclassification on confirmatory biopsy in their institutional AS experience. Among 406 men with Grade Group 1 cancer who underwent confirmatory biopsy, 85 (21%) were reclassified to Grade Group ≥2. Multivariable analysis demonstrated that older age (odds ratio 1.07, P <0.01) and increased number of positive biopsy cores at diagnosis (odds ratio 1.37, P <0.01) were significantly associated with reclassification at confirmatory biopsy.

Consistent with these observations, previous studies have identified tumor volume (eg number or percentage of positive biopsy cores, bilateral cancer) as a risk factor for reclassification.[1-3] Similarly, while the practical utility of PSA and PSA kinetics appear limited in this setting,[4] measures of PSA likely do provide some additional information. In recent years, older age has been identified as a significant risk factor for biopsy reclassification in multiple AS cohorts.[5-8] The present analysis corroborates these findings that older men do, in fact, appear to be at increased risk of reclassification during AS. This represents a significant paradigm shift given that surveillance was initially considered a more reasonable strategy for older men.

These data yield many important practical and disease-specific questions. Practically, the frequency with which reclassification results in long-term adverse outcomes (eg metastatic disease, cancer-specific mortality), particularly in an older population, is likely to be limited. On the other hand, population-based data reveal that older men diagnosed with prostate cancer account for a disproportionately high rate of metastatic disease, and cancer-specific mortality, despite a higher risk of death from competing causes.[9] Finally, what is the biological mechanism underlying this relationship? Is it possible that decreased immunity with older age may account for these findings?[10] Understanding the biological mechanism of this relationship in the AS setting may provide insight as to the varied clinical aggressiveness of prostate cancer in general. For example, if reduced tumor immunity in older men contributes to progression on AS, could similar, individual-level variation in tumor immunity contribute to the wide range of cancer aggressiveness observed in the overall population?

Certainly, the intensity with which to monitor patients on AS merits a careful consideration of available data and patient-specific preferences. The current findings provide additional insight as we aim to advance toward more data-driven, risk-adapted surveillance strategies incorporating known risk factors. Ultimately, understanding the genetic and molecular changes that underlie the wide-ranging clinical behavior of prostate cancer remains a key step toward optimizing management of all patients diagnosed with this disease.

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