More than 1 million prostate biopsies are performed annually in the United States, predominantly driven by elevations in PSA. The merits of PSA screening have been widely debated due largely to its low specificity for prostate cancer (PCa) , especially for high-grade disease.

Two randomized trials (PLCO/ERSCP) failed to resolve the controversy and the U.S. prostate screening task force (USPSTF) recently gave PSA screening a Grade D, recommending against it. In doing so the USPSTF failed to fully acknowledge the limitations and merits of both the PLCO and ERSCP trials and dismissed the fact that over the past 20 years of PSA-based screening, PCa-specific mortality has been reduced by close to 40%, while the risk of metastatic disease has been substantially reduced (*Urol Onc* 2012;30:117-119).

Given the need to reduce overdiagnosis of low-stage/low-grade PCa while improving detection of aggressive disease, the American Urological Association, the American College of Surgeons, and National Comprehensive Cancer Network guideline committees have made recommendations for risk-adjusted PSA screening, citing data demonstrating that PSA baselining and kinetics dramatically improve screening efficiency, particularly in younger populations.

Nonetheless, in the absence of widespread adoption of risk-adjusted and patient-informed screening strategies, a likelihood of over- and underdiagnosis and over- and undertreatment exists, with attendant morbidities pending improved diagnostic tests.

Among the most promising new molecular tests for PCa screening is PCA-3, a non-coding, large-chain RNA over-expressed in PCa. PCA3 is detectable in urine and independent of prostate size and PSA.

In a recent study led by the National Cancer Institute Early Detection Research Network and presented last month at the American Association for Cancer Research, Wei and colleagues reported on a comprehensive, prospective, independent validation of urinary PCA3 alone or in combination with common clinical factors (prior negative biopsy, PSA, race, age, abnormal DRE, and family history) for the detection of PCa at 11 U.S. sites.

In nearly 1,000 men undergoing initial or repeat biopsy, these investigators found that urinary PCA3 prior to a prostate biopsy improved the prediction of PCa and high-grade disease with a high positive predictive value (90%) in the initial biopsy setting and a high negative predictive value (88%) in the repeat biopsy setting. The investigators conclude that counseling men undergoing prostate biopsy in the context of PCA3 would reduce the burden of prostate biopsies.

While widespread adoption of urinary PCA-3 has not yet been incorporated into most physician screening practices, it represents a clear positive step toward a more risk adjusted biopsy strategy, a goal on which we all can agree.

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