

PROSTATE CANCER

Four-kallikrein panel to reduce unnecessary prostate biopsy

PSA screening is widely used to detect prostate cancer. After 9 years of follow-up, the European Randomised Study of Screening for Prostate Cancer showed that PSA testing resulted in a 20% reduction in the number of prostate cancer deaths. In the US, these impressive results have contributed to widespread uptake of PSA testing by older men; approximately 75% of men aged 50 years or more have had at least one PSA test.

Unfortunately, not all news regarding PSA screening is good. While it has undoubtedly saved lives, this comes at a high cost in terms of money, unnecessary biopsies and overdiagnosis, which is a particular problem as it can lead to unnecessary treatment of indolent disease.

These limitations have led researchers from the Memorial Sloan–Kettering Cancer Center to attempt to use additional molecular markers to improve the specificity of PSA. Their test, described as the four-kallikrein

panel, assays the blood levels of the three subtypes of PSA (complex, intact and nicked) and hK2, a molecule involved in PSA activation. Andrew Vickers, first author of the study, explains: “We hypothesized that measuring the different forms of PSA separately, rather than lumping them together, and additionally measuring hK2, would allow us to better predict which men with elevated total PSA [would have] biopsy-detectable prostate cancer.”

The group had previously demonstrated in a small patient sample that this hypothesis was valid, but they needed to establish it using the gold standard of a large, independent, representative, population-based cohort with biopsy results. This cohort included a training set of frozen samples, collected from 728 men, and a validation set of samples from 2,186 men, all of whom had total serum PSA levels of at least 3 ng/ml.

As expected from the previous results, the addition of the subtypes of PSA and

hK2 to a model containing total PSA levels and age significantly improved the AUC. Vickers comments: “The panel of markers was much better able to predict the result of biopsy than PSA alone.”

To put this finding into context, in 1,000 men, this improvement in prediction accuracy would result in 513 fewer biopsies being performed and 300 cancers being detected. Although 66 men with cancer would be advised not to have a biopsy, these would be predominately low-grade tumors.

If these results are validated in other cohorts as planned by Vickers’ team, this test could be implemented with no change to clinical practice and result in a reduction in unnecessary biopsies and possibly also overdiagnosis.

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Original article Vickers, A. *et al.* Reducing unnecessary biopsy during prostate cancer screening using a four-kallikrein panel: an independent replication. *J. Clin. Oncol.* **28**, 2493–2498 (2010)