SCREENING

Four-kallikrein panel to reduce unnecessary prostate biopsy

Prostate-specific antigen (PSA) screening is an accepted method for the detection of prostate cancer. After 9 years of follow up the use of this test has resulted in a 20% reduction in the number of prostate cancer deaths. In the USA, these impressive results have played their part in the fact that approximately 75% of men older than 50 years have had at least one PSA test.

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

These limitations have led researchers from the Memorial Sloan–Kettering Cancer Center to attempt to use additional molecular markers to improve this widespread tool. 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, explained "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 had 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 taken from 728 men and a validation set from 2,186 men, all with 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 (an indication of improvement in model quality). 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 detected, and although 66 men with cancer would be advised not to have a biopsy these would be predominately the low-grade cancers associated with overdiagnosis.

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)