Nature Reviews Urology | Published online 24 November 2015; doi:10.1038/nrurol.2015.286

PROSTATE CANCER

STHLM3 model for prostate cancer screening

> "...use of the STHLM3 model would have reduced the total number of biopsies by 32% and the number of benign biopsies by 44%"

A new screening model could improve the identification of high-risk prostate cancer in men aged 50–69 years, while reducing the number of unnecessary biopsies in those with clinically insignificant disease, say researchers.

Serum PSA level is widely used as a screening test for prostate cancer, but its poor specificity leads to many unnecessary prostate biopsies and the overdiagnosis of low-risk prostate cancer. Many single nucleotide polymorphisms (SNPs) have been identified to be associated with prostate cancer, and it has been suggested that combining PSA level with a genetic score based on these SNPs could increase the specificity of prostate cancer testing. In their new study, Grönberg and colleagues investigated whether the Stockholm 3 (STHLM3) model (which combines serum PSA level, levels of other plasma protein biomarkers, SNPs and clinical variables such as age and family history) could improve the specificity of detection of high-risk prostate cancer and reduce the proportion of men undergoing prostate biopsy.

The study was a prospective, population-based study of Swedish men without prostate cancer who were aged 50–69 years. Grönberg *et al.* used a 'training' cohort of 11,130 men to train and predefine the STHLM3 model algorithm, and a 'validation' cohort of 47,688 men to prospectively test the algorithm. PSA levels were measured in all patients and the additional biomarkers were analysed in men with a PSA concentration of ≥1 ng/ml. Men with a PSA concentration of ≥3 ng/ml or an STHLM3 model indicating high risk were referred to a urologist for digital rectal exams, prostate volume measurements and transrectal prostate biopsy.

The researchers report that the STHLM3 model performed significantly better than did PSA concentration alone for the detection of high-risk (Gleason score ≥7) prostate cancer (areas under the curve 0.74 versus 0.56; $P<0.0001$). All of the variables used in the STHLM3 model were shown to be significantly associated with high-risk prostate cancer. Using a cutoff at the same level of sensitivity as for a PSA test of ≥3 ng/ml for detecting high-risk prostate cancers, Grönberg *et al.* report that use of the STHLM3 model would have reduced the total number of biopsies by 32% and the number of benign biopsies by 44%.

"We have shown that a combination of plasma protein biomarkers, genetic polymorphisms, and clinical variables can improve the specificity of prostate cancer screening significantly compared with PSA in men aged 50–69 years," say the authors. "Use of the STHLM3 model in structured screening could reduce the number of prostate biopsy samples taken by about a third compared with the use of PSA screening. Importantly, this can be achieved without compromising the number of high-risk cancers diagnosed."

Rebecca Kelsey

ORIGINAL ARTICLE Grönberg, H. *et al.* Prostate cancer screening in men aged 50–69 years (STHLM3): a prospective population-b ased diagnostic study. *Lancet Oncol.* http://dx.doi.org/10.1016/S1470-2045(15)00361-7