P09 Mass spectrometry based urinary biomarkers to distinguish non-significant from significant prostate cancer

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Introduction & Objectives: Prostate cancer (PCa) is progressing slowly when present in low risk forms but can be lethal when it progresses to metastatic disease. Guidance on intervention by a non-invasive test is needed to reduce unnecessary and invasive biopsies.
Aimed at improving on the current discrimination of significant PCa, capillary-electrophoresis coupled to mass spectrometry (CE-MS) was employed to identify peptides specific for PCa in urine samples from patients with clinically significant and non-significant disease.

Materials & Methods: A case–control study was performed on patients who underwent a transrectal ultrasound (TRUS)-guided biopsy in the Urology department of Reina Sofia Hospital, in Cordoba, as part of the ONCOVER project. Approval was obtained by Reina Sofia Hospital Research Ethics Committee. 823 patients with low levels of PSA (<15ng/ml) were considered, donating urine samples prior to biopsy according to clinical practice.
A training set of 543 patients (98 with significant and 445 with non-significant PCa) and a validation set of 280 patients (48 with significant and 232 with non-significant prostate cancer) were employed. Statistical comparison was performed in the training set by Wilcoxon test and adjustment for false discovery rate was applied by Benjamini Hochberg. A frequency threshold of 70% was set and the analysis was repeated 5 times (by randomly discarding 30% of patients in each group).19 significant peptides were subsequently combined by a support vector machine algorithm (SVM).

Results: An SVM model including the 19 significant peptides was optimized (c=1280, g=0.0012) in the training set of 543 patients. Validation of the 19-peptide SVM model in 280 patients resulted in AUC of 0.81 [0.76-0.86; 95% confidence interval (CI)], outperforming PSA (AUC= 0.58; 0.52-0.64; 95% CI) and the ERSPC risk calculator (AUC= 0.69; 0.63-0.70; 95% CI).
Among the 19 peptide biomarkers, the majority originated from alpha-1 collagen of types (I), (XI), (XVII), (XXI) and alpha-2 type (I), (V), (IX). Within those, a unique motif (pGP) was very prominent, which upon proteolytic cleavage by matrix metalloproteinases, binds to (C–X–C motif) receptors and is associated with neutrophil attraction. Other biomarkers were fragments of protein phosphatase 1 regulatory subunit 3A, chemokine (C-X3-C motif) ligand 1 and Semaphorin-7A.

Conclusions: In this study, a non-invasive urinary-based test for detecting significant prostate cancer was developed and validated including 823 patients with low levels of PSA (< 15ng/ml).The overall performance of the test is 90% sensitivity and 59% specificity.
Implementation of such a test as a guide to biopsy could decrease the number of invasive biopsies. Additional correlation of the urinary profiles with the prostatectomy outcome is currently ongoing and validation of the urinary markers in a prospective investigation is also planned.