Using a combination of plasma and urine biomarkers along with serum PSA in predicting prostate cancer and screening for high-risk cancer.

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Background: We have previously reported algorithms which combine urine and plasma biomarkers to provide diagnostic information regarding a decision to perform a prostate biopsy and biologic stratification of aggressive prostate cancer (PCa). We expanded our biomarker panel to explore the potential of incorporating androgen receptor (AR) and PTEN expression levels in urine and plasma to improve our algorithms’ ability to: 1) Determine the presence of PCa in patients with presumed benign prostate hyperplasia (BPH), and to: 2) Distinguish high- vs. low-risk PCa.

Methods: We measured the mRNA levels of UAP1, PDLIM5, IMPDH2, HSPD1, PCA3, PSA, TMPRSS2, ERG, GAPDH, B2M, AR, and PTEN in plasma and urine. Patient age, serum PSA (sPSA) level, and PCR data were used to develop algorithms. Gleason Score (GS) <7 is used as the indicator for low-risk PCa. Approximately two thirds of patients (190/287) were used as the training set.

Results: In a cohort of 287 patients undergoing prostate biopsy, results demonstrated that 103 (36%) showed BPH and 184 (64%) had PCa. Of these patients with PCa, 107 (58%) had high-risk PCa (GS≥7). Using our biomarker algorithm, the area under the receiver operating characteristic curve (AUROC) for distinguishing PCa from BPH was 0.87. The model sensitivity was 76% and specificity of 71%, using the testing set. A second algorithm for predicting high-risk PCa (GS ≥7) vs. GS <7 cancer or BPH demonstrated an AUROC of 0.80. This algorithm demonstrated a specificity of 76% and a sensitivity of 44% in the testing set. Patients with concordant results showed specificity of 89% and sensitivity of 59% for having high-grade aggressive PCa, and specificity of 94% and sensitivity of 81% for having PCa and not BPH, but with tolerating the non-detection of low-risk PCa. Combining the two algorithms and accepting a diagnosis of PCa if one of the two algorithms was positive for cancer, regardless of the aggressiveness, showed specificity and sensitivity of 82% and 92% respectively, with the possibility of missing low-risk cancer.

Conclusions: Adding AR and PTEN to other biomarkers can significantly improve the value of serum PSA in predicting and screening for PCa as well as detecting high-risk PCa.

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