

PCA3: A Urine-Based Genetic Assay for Detection of Prostate Cancer in Men with Elevated PSA

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Background: Currently, early detection of prostate cancer relies primarily on an abnormal digital rectal examination (DRE) and an elevated prostate-specific antigen (PSA) level leading to a prostate biopsy. However, because of low positive predictive values, up to 75% of men with elevated PSA and/or suspicious DRE have a negative biopsy. We investigated the value of a new molecular marker--PCA3 in predicting the likelihood of prostate cancer.

Methods: We undertook a prospective, multi-practice, community-urologist-based, and IRB approved clinical trial to evaluate PCA3. Urine samples were obtained from 974 men with elevated serum PSA (≥ 2.5 ng/ml) and/or abnormal digital rectal examination prior to routine minimum 10-core prostate biopsy following standard study protocol in 30 medical practices. Urine samples were processed within 48 hours of collection. PCA3 and PSA mRNA were isolated, amplified and quantified by magnetic target capture, transcription-mediated amplification, and chemiluminescent hybridization protection assay technologies. The PCA3 value was determined using the ratio of PCA3 mRNA copy number to the PSA mRNA copy number multiplied by 1,000.

Results: In total, 380 of 974 patients (39%) were diagnosed with prostate cancer, with a mean Gleason score of 7 (range, 6-9) and 26% (range 1-100%) of the biopsy specimens involved by cancer. An additional 106 cases (11%) had only high-grade PIN and/or atypical small acinar proliferation suspicious for cancer (ASAP), and 488 cases (50%) were benign. The mean PCA3 value in men with prostate cancer was significantly higher than in those without cancer (48 vs. 26, $p < 0.0001$). PCA3 score was associated with the presence of cancer ($p < 0.0001$) and Gleason score ($p=0.0001$), but was not associated with cancer volume ($p=0.56$). Using a cutoff value of 35, PCA3 had an odds ratio of 2.6 for predicting prostate cancer. PCA3 had a specificity of 77% and a sensitivity of 44% for the diagnosis of prostate cancer, while the specificity and sensitivity for serum PSA were 22% and 87%, respectively.

Conclusion: We found that the PCA3 urine test significantly improved the specificity for the detection of prostate cancer compared to serum PSA. Further evaluation of this urinary marker in screening for prostate cancer appears indicated.