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Diagnostic performance of PCA3 and TMPRSS2:ERG biomarkers in prostate cancer patients urine collected with and without prostate massage

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Introduction & Objectives: PCA3 and TMPRSS2:ERG are well defined prostate cancer biomarkers that can be detected non-invasively in patients urine. The goal of this study is to assess diagnostic performance of PCA3 and TMPRSS2:ERG biomarkers in combination with standard clinical information in patients urine specimens collected with and without prostate massage (DRE) for prognosis of positive biopsy (Bx) and Gleason ≥7 (GS7+) positive biopsy.

Materials & Methods: The study comprises a total of 295 urine samples without DRE and 303 samples after DRE received from informed and consented patients indicated for first or repeat prostate biopsy. Only subjects with PSA levels 2-10 ng/mL were chosen for study. Urine was collected using first void urine collection device with urine stabilization solution. Amounts of PCA3 and TMPRSS2:ERG RNAs in extracted nucleic acids was detected by RT-qPCR and biomarker scores against KLK3 RNA were calculated. Logistic regression models were created by combining log transformed values of biomarker scores, PSA density and untransformed values of patients age for both patient groups. Models were evaluated by estimating diagnostic parameters values and a fraction of avoided biopsies at chosen cutoff values whereas sensitivity of test was kept close to 90%. In addition, bootstrap optimism-corrected AUC values were calculated from Somers' D statistics as given by validate function from rms package in R environment with 1000 bootstrap replicates.

Results: PCA3 and TMPRSS2:ERG biomarkers in combination with PSA density and patients age demonstrated high diagnostic performance (AUC) for both prostate cancer and high grade (GS7+) prostate cancer in urine without DRE. After the DRE diagnostic performance, specificity and NPV of the tested biomarkers was higher.

Biomarkers and parameters	Patients (Negative Bx/Positive Bx)	Prognosis	DRE	AUC	Sensitivity	Specificity	NPV	PPV	Avoided Biopsies
PCA3, TMPRSS2:ERG, PSA density, age	295 (146/149)	Positive Bx	NO	71%	90%	33%	78%	57%	21%
	295 (70/225)	GS7+ Positive Bx	NO	74%	90%	43%	93%	33%	35%
	303 (153/150)	Positive Bx	YES	78%	90%	43%	81%	62%	26%
	303 (71/232)	GS7+ Positive Bx	YES	79%	89%	55%	94%	38%	45%

Conclusions: Testing of PCA3 and TMPRSS2:ERG biomarkers in patients urine can be used for biopsy outcome prognosis. Positive biopsy and GS7+ positive biopsy can be accurately prognosed in both simple urine and urine after DRE and would let avoid up to 45% unnecessary biopsies.