10 Urinary 3-gene methylation test for prostate cancer risk assessment

European Urology Supplements 2019;18(3):e2435

Bakavicius A.[1] , Daniunaite K.[2] , Jarmalaite S.[3] , Jankevicius F.[1]

[1]Clinic of Gastroenterology, Nephrourology and Surgery, Institute of Clinical Medicine of the Faculty of Medicine of Vilnius University, Vilnius, Lithuania, [2]Life Sciences Centre, Vilnius University, Vilnius, Lithuania, [3]National Cancer Institute, Research Centre, Vilnius, Lithuania

Introduction & Objectives: PCa treatment selection mostly depends on tumour biopsy-based Gleason score and clinical tumour stage. Pathologic upgrading and upstaging have emerged as a serious issues in PCa patients and were reported to be associated with an increased risk of BCR so inferior cancer-specific survival rates.
In the present study we assessed the performance of established clinical predictors of outcome, and DNA methylation of three tumour suppressor genes, RARB, RASSF1 and GSTP1 – as potential noninvasive biomarkers for more accurate PCa risk assessment.

Materials & Methods: In total, 1056 treatment-naïve patients with histologically confirmed PCa who underwent RP at Vilnius University Hospital Santaros klinikos between January 2008 and December 2014 were included. Previous ADT, AS and history of urothelial Ca were considered as exclusion criteria. Upgrading was defined as any increase of ISUP grade group between biopsy and RP pathology, whereas upstaging was confirmed if a patient was pathologically diagnosed with ≥pT3 when clinically unsuspected. In total, 514 urine samples (188 voided and 326 catheterized) from these patients were available for DNA methylation analysis using qualitative methylation-specific PCR.

Results: Upgrading was observed in 27% of patients, while 20% of patients upstaged post-RP, with total misclassification rate of 39%. Among the upgraded cases, 86% of patients were initially diagnosed with ISUP grade group 1 disease. Patients initially diagnosed with cT1c PCa dominated among upstaged cases (49%). According to risk stratification 23.9% of patients were assigned to a higher PCa risk than clinically suspected, of whom 69% had been preoperatively diagnosed with low-risk disease. Upgrading only was the major cause of the risk increase (45%).
Methylation frequencies were similar between voided and catheterized urine cohorts, except for GSTP1 which was more common in voided urine (P=0.016). The average methylation levels were similar in both cohorts, except higher methylation level of RASSF1 was observed in catheterized urine. In ROC analysis, 3-gene set alone and in combination with PSA significantly predicted PCa upgradingin voided (AUC=0.60 for 3-gene set, AUC=0.61 for complemented with PSA) and catheterized (AUC=0.60 for 3-gene set, AUC=0.70 for complemented with PSA) urine samples (all P<0.050). While upstaging was predicted by 3-gene set complemented with PSA in voided (AUC=0.61) and catheterized (AUC=0.63) urine samples (all P<0.050). 3-gene test together with PSA was able to predict risk change when catheterized urine was used (AUC=0.60, P=0.028) and with the borderline significance in voided urine.

Conclusions: Currently available diagnostic tools do not allow precise preoperative PCa risk assessment, especially in low-risk PCa. Combination of the urinary 3-gene test and serum PSA can improve individual risk assessment at most critical point, when the most appropriate treatment modality should be selected.