Radical prostatectomy outcomes from a validated urine exosome gene expression assay which predicts high-grade (GS7) prostate cancer suggests utility for men enrolled in Active Surveillance

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Introduction:

With over-diagnosis and overtreatment of indolent prostate cancer (PCa), non-invasive screening tools that predict low-grade (≤ Gleason score 6, GS 6) from high-grade (≥ GS 7) PCa will play a significant role in the treatment decision process. Recently, we demonstrated that the urine exosome gene expression assay ExoDx™ Prostate(IntelliScore) (Figure 1A) could discriminate high-grade (≥ GS 7) from low-grade (GS 6) and benign disease biopsy outcomes, and could potentially reduce the number of unnecessary biopsies (Figure 1B, Table 1) [1]. In a parallel study, we also showed that EPI scores were associated with pathologic stage (IP) and radical prostatectomy Gleason score (RP-GS). We now sought to expand these results and further examine outcomes from men enrolled in the EPI validation trial who had selected surgery.

Methods:

Urine was collected from a total of 242 patients prior to scheduled radical prostatectomy (RP). The pre-RP EPI score was generated and the tissue status from both a pre-RP biopsy and from final pathology post RP using the ISUP 2014 criteria [2] were reported. Additionally, RP-GS outcomes from 86 men that were enrolled in the 519-patient validation cohort were evaluated [1]. The patients were derived from the two cohorts as follows: 242 patients from a dedicated pre-RP study (previously reported) and 86 patients from the EPI validation study, who proceeded to have a RP. Both patient cohorts were merged prior to final analysis (N=328). During pathology evaluation of the prostate after RP, patients often experience up- and down-grading relative to their biopsy status. In this analysis, we are focusing on a subset of 112 out of 328 men with an initial biopsy status of ISUP 1 (i.e. potential candidates for Active Surveillance). We reviewed EPI scores and PSA values for those patients that were ISUP1 by biopsy with their RP pathology outcomes:

Results:

The pre-RP cohort (N=242) segregates into 33% ISUP 1 (GS 6), 42% ISUP 2 (GS 3+4) and 25% > ISUP 2 (GS ≥ 5+3) patients prior to RP. Comparable ISUP ratios are observed in the EPI-validation cohort (N=86) with 38% ISUP 1, 34% ISUP 2 and 28% > ISUP 2, respectively. 33% of the pre-RP patients exhibited up-grading while 14% were down-graded and 26% of the EPi-validation patients were up- and down-graded. Overall demographic properties of the merged patient cohort (N=328) are shown in Table 3.

Conclusion:

The EPI test is a non-invasive, non-DRE gene expression signature that accurately discriminates low-grade from high-grade PCa in ISUP and traditional Gleason score based grading systems. Improved discrimination for predicting higher ISUP groups suggests a potential role in longitudinal monitoring of patients enrolled in Active Surveillance and warrants further validation.

References:


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EPI scores and PSA values were obtained from all 328 patients. Subsequent analysis focuses on a subset of 112 low-grade PCa patients that were classified as ISUP 1 based on biopsy outcome (Figure 2). Higher urine EPI scores are associated with higher RP-ISUP groups (Figure 3A). Patients initially classified as ISUP 1 that were re-classified as > ISUP 2 after RP have significantly higher EPI scores (p-value: 0.001) compared to patients that were not up-graded after RP. In contrast, PSA was not able to discriminate the different patient groups. The distributions of PSA values are very similar between up- and non-up-graded patients (Figure 3 B).