Association of PSA and number of cores positive with likelihood of adverse pathology at radical prostatectomy based on a 17-gene expression assay.

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Background: The overtreatment of prostate cancer and underutilization of active surveillance in men with Gleason 6 (GS6) cancer stems from uncertainty with current risk instruments such as volume of GS6 tumor and PSA > 10 ng/ml. The 17-gene biopsy-based RT-PCR assay has been analytically and clinically validated as an independent predictor of adverse pathology at prostatectomy. We report on the impact of volume of GS6 disease and PSA at biopsy on the biologic aggressiveness of the disease as measured by the assay (GPS). Methods: 1,055 pathology reports received at Genomic Health, Inc. were reviewed to record GS, number of cores positive, and PSA. GPS was calculated from a single block for each case with an associated path report using the validated algorithm of 12 cancer and 5 reference genes; median GPS was calculated for each sub-group (≤ 2 cores positive, > 4 cores positive, PSA < 4 ng/ml, PSA 4-10 ng/ml, PSA > 10 ng/ml). Results: 803 cases (76%) were submitted as GS6. 66% of cases contained 12 cores, 4% of cases had < 12 cores and 30% of cases had > 12 cores. The median GPS for GS6 cases with ≤ 2 cores positive was 24 (IQR 16.5 to 30.5) compared to a median GPS of 26 (IQR 20 to 34) for 4 or more cores positive. After incorporating the GPS, risk refinement, a change in categorical risk assessment was seen in 24% of cases with ≤ 2 cores positive and 26% of cases with > 4 cores positive. 294 of cases with GS6 also reported a PSA value. 25% of GS6 cases had a PSA < 4, 67% were 4-10, and 8% were > 10 ng/ml. No significant correlation was seen between PSA and GPS. The median GPS values for cases with a PSA < 4, 4-10, and > 10 were 25(IQR 16-31), 24(IQR 17-32), and 25(IQR 17-39), respectively. Risk refinement following GPS occurred in 48% of cases with a PSA < 10 and 23% with a PSA > 10. Conclusions: The GPS results highlight the broad spectrum of tumor aggressiveness in a series of 803 biopsies containing GS6 independent of % cores positive and PSA. The degree of risk refinement among all GS6 cases independent of tumor volume or PSA highlight the utility of the GPS to provide predictive information beyond traditional clinical variables used for risk stratification in the management of men with GS 6 disease at the time of diagnosis.