Patient-specific meta-analysis (MA) of two validation studies to predict pathologic outcomes in prostate cancer (PCa) using a 17-gene genomic prostate score (GPS).

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Background: We validated a biopsy-based assay as a predictor of PCa aggressiveness in two independent patient cohorts. Using GPS with NCCN risk group, the test provides an estimate of likelihood of favorable pathology (LFP) in low-intermediate risk PCa based on data from the first validation study. The second study re-confirmed the association between GPS and LFP. We combined information from both studies to provide more precise estimates of LFP, and examined predictive models using GPS with other clinical risk tools.

Methods: Patient-specific MA provides precision-weighted predictions for individual patients using data from multiple studies (Crager and Tang, J. Appl. Stat.2014). MA was performed on the two validation studies (732 patients total) using GPS (scale 0-100) with CAPRA score, NCCN risk group, or AUA/EAU risk group as predictors of LFP (Gleason score 3+3 or 3+4, organ-confined disease). Decision curves were calculated using the MA risk estimates.

Results: MA provided more precise estimates of LFP with narrower confidence intervals (CIs) than either study alone (median width 24% narrower than the smaller of the two individual study CIs). GPS added significant predictive value for LFP to each of the 3 clinical classifiers. A model utilizing GPS and CAPRA provided the most risk discrimination. In decision-curve analysis, greater net benefit was shown when combining GPS with each clinical classifier compared with the clinical classifier alone. Over a wide range of threshold probabilities, incorporation of GPS would be expected to lead to fewer treatments of patients with favorable pathology without increasing the number of patients with adverse pathology left untreated. The proportion of men with MA-estimated LFP > 80% was 31% with GPS and CAPRA, and 23% with GPS and NCCN risk group; 11% were identified with LFP > 80% using NCCN risk group alone.

Conclusions: Patient-specific MA of two independent studies provided more precise risk estimates reflecting the complete body of evidence. GPS adds predictive value to three clinical risk tools. The MA-estimated LFP identified more patients with an LFP > 80% than identified by clinical classifiers alone.