

Multimodal Risk Stratification in Prostate Cancer Using Digital Pathology Artificial Intelligence and Genomic Classification

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ABSTRACT

Background:

The heterogeneity of outcomes for prostate cancer necessitates inspired the development of gene expression classifiers and digital pathology-based artificial intelligence (DPAI) tools. However, the utility of DPAI tools in the context of clinical, pathologic, and genomic information is currently unknown.

Methods:

The primary objective was to develop and determine the prognostic performance of newly generated biopsy and radical prostatectomy (RP)-derived DPAI models in the context of clinicopathologic variables and the 22-gene Decipher genomic classifier (GC). Between 2016-2024 patients with non-metastatic prostate cancer were assessed from the prospective Genomics Resource for Intelligent Discovery (GRID) registry and linked to real-world claim data. A total of 34,698 patients were included (26,025 biopsy and 8,673 RP), of which 1,059 patients developed distant metastatic disease (DM). Patients were divided into development, test, and validation cohorts stratified by DM and baseline clinical genomic variables. Attention-based multiple instance learning models were trained to predict DM. Associations between DPAI, GC, clinicopathologic variables, and DM were evaluated using multivariable Cox regression. Joint stratification by DPAI and GC was assessed across clinical and pathologic risk groups.

Results:

In the validation cohort, using multivariable analysis after adjustment for GC and clinicopathologic factors, higher DPAI scores were associated with increased risk of DM in biopsy (hazard ratio [HR] per standard deviation 1.40, 95% confidence interval [CI] 1.17-1.68) and RP cohorts (HR 1.56, 95% CI 1.30-1.86). DPAI and GC were moderately correlated (Spearman rho 0.48 and 0.59 in the biopsy and RP cohort, respectively). Among patients with NCCN high/very high-risk disease, those with both higher DPAI and higher GC scores had the highest DM risk (5-year DM of 16%), while lower scores were associated with uniformly low DM rates (5-year DM of 5%).

Conclusions:

Our novel DPAI models provide independent prognostic information in the context of the Decipher GC in localized prostate cancer. This enables the use of robust multi-modal models including clinical, pathologic, genomic, and DPAI information to further personalize treatment for prostate cancer patients.