Abstract

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Validation of a genomic classifier that predicts metastasis following radical prostatectomy in an at risk patient population.

Karnes RJ[1], Bergstralh EJ, Davicioni E, Ghadessi M, Buerki C, Mitra AP, Crisan A, Erho N, Vergara IA, Lam LL, Carlson R, Thompson DJ, Haddad Z, Zimmermann B, Sierocinski T, Triche TJ, Kollmeyer T, Ballman KV, Black PC, Klee GG, Jenkins RB.

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Abstract

PURPOSE: Patients with locally advanced prostate cancer after radical prostatectomy are candidates for secondary therapy. However, this higher risk population is heterogeneous. Many cases do not metastasize even when conservatively managed. Given the limited specificity of pathological features to predict metastasis, newer risk prediction models are needed. We report a validation study of a genomic classifier that predicts metastasis after radical prostatectomy in a high risk population.

MATERIALS AND METHODS: A case-cohort design was used to sample 1,010 patients after radical prostatectomy at high risk for recurrence who were treated from 2000 to 2006. Patients had preoperative prostate specific antigen greater than 20 ng/ml, Gleason 8 or greater, pT3b or a Mayo Clinic nomogram score of 10 or greater. Patients with metastasis at diagnosis or any prior treatment for prostate cancer were excluded from analysis. A 20% random sampling created a subcohort that included all patients with metastasis. We generated 22-marker genomic classifier scores for 219 patients with available genomic data. ROC and decision curves, competing risk and weighted regression models were used to assess genomic classifier performance.

RESULTS: The genomic classifier AUC was 0.79 for predicting 5-year metastasis after radical prostatectomy. Decision curves showed that the genomic classifier net benefit exceeded that of clinical only models. The genomic classifier was the predominant predictor of metastasis on multivariable analysis. The cumulative incidence of metastasis 5 years after radical prostatectomy was 2.4%, 6.0% and 22.5% in patients with low (60%), intermediate (21%) and high (19%) genomic classifier scores, respectively ($p<0.001$).

CONCLUSIONS: Results indicate that genomic information from the primary tumor can identify patients with adverse pathological features who are most at risk for metastasis and potentially lethal prostate cancer.

KEYWORDS: AUC; BCR; CC; ECE; GC; GPSM; GS; Gleason score; Gleason score, preoperative PSA, SVI, SM; MVA; N+; PSA; RP; SM+; SVI; area under ROC curve; biochemical recurrence; clinical only classifier; extracapsular extension; genomic classifier; lymph node involvement; multivariable analysis; ncRNA; neoplasm metastasis; noncoding RNA; positive surgical margin; prognosis; prostate; prostate specific antigen; prostatic neoplasms; radical prostatectomy; seminal vesicle invasion; transcriptome

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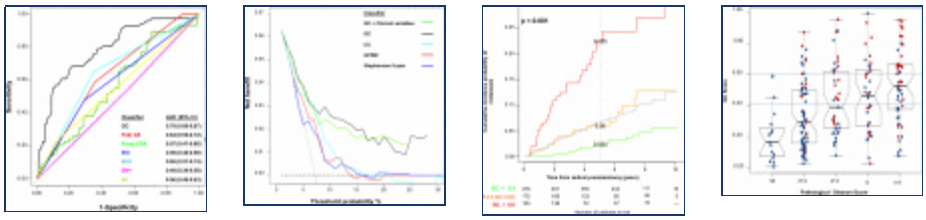

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