Improved prognostic tools for newly diagnosed prostate cancer are needed to more appropriately match treatment to a patient's risk of progression.

The cell-cycle progression (CCP) score is a highly validated RNA expression signature composed of genes involved in CCP.

The CCP score has been combined with CAPRA (CCR, combined clinical cell cycle risk) to generate an estimate of prostate cancer mortality (PCM) within 10-years of diagnosis.

Here, we evaluate how well the prognostic information from CCP can reclassify patients compared to their initial assignment to an AUA risk category based on clinicopathologic features alone.

The CCP score was calculated based on RNA expression of 31 cell cycle progression genes normalized to 15 housekeeping genes.2,12

The CCP score was previously validated and is calculated as a linear combination of the CCP score and CAPRA (0.59 × CAPRA + 0.57 × CCP).

A risk reclassification scheme was applied to patients from two cohorts with long-term follow-up and clinically localized prostate cancer diagnosed by needle biopsy and managed conservatively in the UK (hereafter outcome cohort, N=765).4,14

PCM risk was estimated according to CCR.

Patients were reclassified into AUA risk groups according to the interquartile range (IQR) of the risk predicted by CCR for each AUA risk category.

The same reclassification scheme was applied to a set of patients tested by the Myriad Genetics commercial laboratory (N=3,965).

The reclassification was consistent with the Kaplan-Meier estimates of PCM for each reclassified group (Figure 2).

Table 1. CCR Reclassification of PCM in Outcome Cohort (N=765)4,14

| AUA LOW (n=101) | LOW | 84 (82.3%) | 17 (16.8%) | 0 (0.0%) |
| AUA INTERMEDIATE (n=240) | 38 (15.4%) | 166 (69.1%) | 36 (15.0%) |
| AUA HIGH (n=424) | 3 (0.7%) | 58 (13.7%) | 363 (85.6%) |

Table 2. CCR Reclassification of PCM in Commercial Cohort (N=3,965)

| AUA LOW (n=1748) | LOW | 1,389 (79.5%) | 394 (20.3%) | 5 (0.3%) |
| AUA INTERMEDIATE (n=1,728) | 363 (21.0%) | 935 (54.1%) | 430 (24.9%) |
| AUA HIGH (n=489) | 28 (5.7%) | 89 (18.2%) | 372 (76.1%) |

Table 2 and Figure 1B show the outcomes of a similar analysis of the commercially tested patients (N=3,965). There is no outcome data associated with these commercial samples. 20% of the AUA low-risk men were reclassified to intermediate risk.

46% of the AUA intermediate risk men were reclassified (21% low and 25% high risk).

24% of the AUA high risk men were reclassified (6% low and 18% intermediate).

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The CCP score has been extensively validated and shown to be associated with aggressive disease in diverse patient cohorts and clinical settings.

We have shown that the additional information included in the CCR significantly improves on PCM risk reclassification compared to what is captured by AUA risk categories.

This additional information can be used to more appropriately guide medical management.

REFERENCES


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