PATIENT AUA RISK CLASSIFICATION BASED ON COMBINED CLINICAL CELL CYCLE RISK (CCR) SCORE

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INTRODUCTION

- 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 score) to generate an estimate of prostate cancer mortality (PCM) within 10-years of diagnosis.
- Here, we evaluate how well the prognostic information from CCR can reclassify patients compared to their initial assignment to an AUA risk category based on clinicopathologic features alone.

METHODS

- The CCP score was calculated based on RNA expression of 31 cell cycle progression genes normalized to 15 housekeeping genes.[1,2]
- The CCR score was previously validated and is calculated as a linear combination of the CCP score and CAPRA (0.39 x CAPRA + 0.57 x 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).[3,4] 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).

RESULTS

- Based on clinicopathologic features alone the outcome cohort was classified according to AUA Guidelines as low (N=101), intermediate (N=240) or high risk (N=424).
- Table 1 and Figure 1A show the reclassification of PCM based on CCR in the outcome cohort.
  - 17% of the AUA low risk men were reclassified to intermediate risk.
  - 31% of the AUA intermediate risk men were reclassified (16% low and 15% high risk).
  - 14% of the AUA high risk were reclassified to intermediate risk.
- The reclassification was consistent with the Kaplan-Meier estimates of PCM for each reclassified group (Figure 2).
- 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% to high risk).
  - 24% of the AUA high risk men were reclassified (6% low and 18% intermediate).

Table 1. CCR Reclassification of PCM in Outcome Cohort (N=765)[3,4]

	LOW	INTERMEDIATE	HIGH
AUA LOW (n=101)	84 (83.2%)	17 (16.8%)	0 (0%)
AUA INTERMEDIATE (n=240)	38 (15.8%)	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)

	LOW	INTERMEDIATE	HIGH
AUA LOW (n=1,748)	1,389 (79.5%)	354 (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%)

Figure 1A. CCR Reclassification of PCM in Outcome Cohort (N=765)

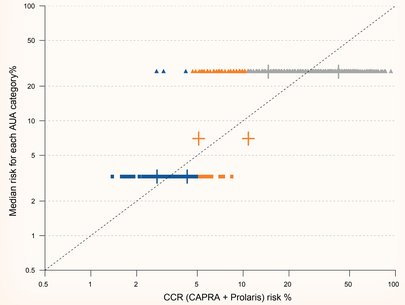
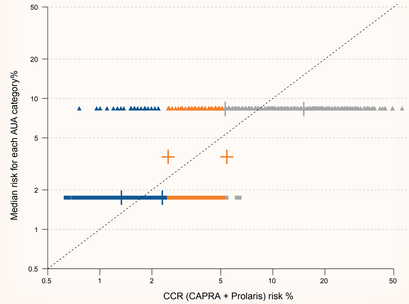
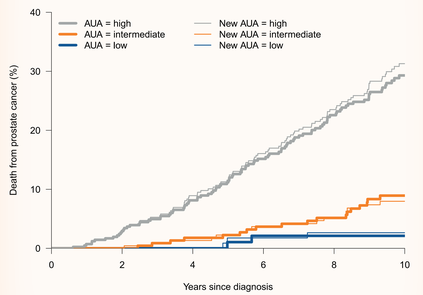


Figure 1B. CCR Reclassification of PCM in Commercial Cohort (N=3,965)



Scatter plot showing the predicted risk of PCM based on clinicopathologic features alone (y-axis) versus CCR risk (x-axis). IQR is indicated by vertical bars for low (blue), intermediate (orange), and high (gray) risk patients.

Figure 2. Kaplan-Meier Estimates of PCM According to AUA Risk Category



CONCLUSIONS

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