Patient Risk Reclassification Based on Combined Clinical Cell Cycle Risk (CCR) Score

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BACKGROUND

- 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 was developed and validated against clinical outcomes (BCR, metastases, mortality) to provide prognostic information to prostate cancer patients in all risk groups.[1-7]
- This molecular information has recently been combined with clinical information (CAPRA)[8] to estimate prostate cancer mortality within 10-years of diagnosis.
- This combined clinical cell cycle risk (CCR) score has been shown to provide improved prognostic information relative to clinical features alone.[5]
- Here we evaluate how the CCR score can reclassify PCM-risk for men tested within the AUA Western section relative to NCCN and AUA risk categories.

METHODS

COHORT

- Prostate biopsy samples from 4,568 men within the AUA Western section were submitted for commercial testing between July 2012 and December 2016.
- Clinicopathological data was obtained from physician-completed test request forms (TRFs).

CCP TESTING

- FFPE biopsy samples were analyzed for the expression of 46 genes (31 CCP genes and 15 housekeeping genes).[3]
- The CCP score is an unweighted average of the CCP genes normalized by the average expression of the housekeeping genes.
- The CCR score is calculated as a linear combination of CAPRA and CCP score (0.39 x CAPRA + 0.57 x CCP).[2]

ANALYSIS

- Patients were assigned to NCCN and AUA risk categories using clinicopathologic data from the TRF.
- Interquartile ranges (IQR) for each NCCN/AUA risk category were determined from the full commercial cohort (N=20,958).
- Patients whose CCR-based PCM risks were outside the IQR of their NCCN/AUA risk category were reclassified according to whether their PCM risk fell within the IQR of another risk category.

RESULTS

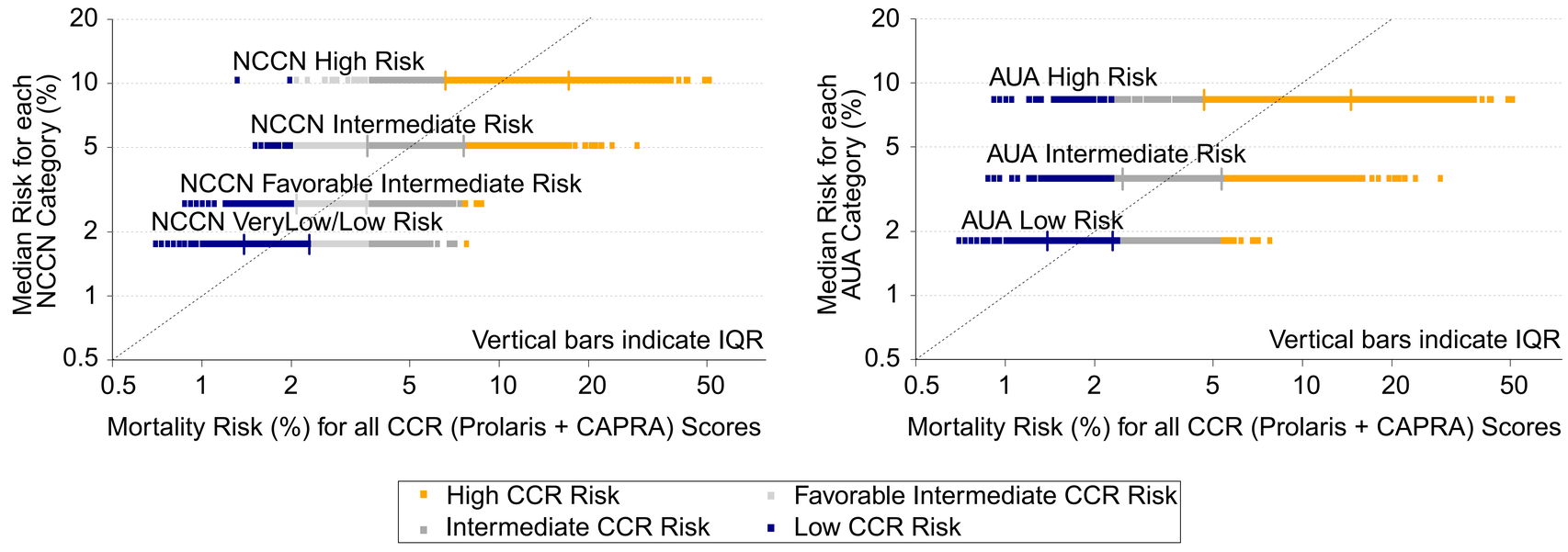
Table 1. Reclassification relative to NCCN risk categories

	CCR Risk Category			
NCCN Risk Category	Low	Favorable Int.	Int.	High
Very Low/Low (n=2277)	1661 (72.9%)	493 (21.7%)	122 (5.4%)	1 (<0.1%)
Favorable Int. (n=981)	242 (24.7%)	501 (51.1%)	232 (23.6%)	6 (0.6%)
Intermediate (n=898)	26 (2.9%)	187 (20.8%)	455 (50.7%)	230 (25.6%)
High (n=412)	2 (0.5%)	18 (4.4%)	94 (22.8%)	298 (72.3%)
Total	1931 (42.3%)	1199 (26.2%)	903 (19.8%)	535 (11.7%)

Table 2. Reclassification relative to AUA risk categories

	CCR Risk Category		
AUA Risk Category	Low	Int.	High
Low (n=2285)	1756 (76.8%)	514 (22.5%)	5 (1.3%)
Intermediate (n=1739)	332 (19.1%)	983 (56.5%)	48 (25.8%)
High (n=544)	50 (9.2%)	91 (16.7%)	49 (80.3%)
Total	**2138 (46.8%)**	**1588 (34.8%)**	**102 (16.1%)**

Figure 1. Risk Reclassification of PCM in Commercial Cohort Using the CCR Score



- Based on clinicopathologic features alone, men in this cohort were classified according to NCCN guidelines (Table 1).
- After calculating PCM-risk based on CCR, 36.2% of men were reclassified to a different risk category relative to NCCN criteria . (Table 1, Figure 1)
  - 12.5% were downgraded
  - 23.7% were upgraded
- Similarly, men were classified according to AUA guidelines according to clinicopathologic features alone (Table 2).
- PCM-risk based on CCR scores resulted in the reclassification of 31.2% of men relative to AUA criteria. (Table 2 and Figure 1)
  - 10.4% were downgraded
  - 20.9% were upgraded

CONCLUSIONS

- The prognostic information in the CCR score results in significant risk reclassification for all patients with localized disease when compared to stratification based only on clinicopathologic criteria.
- This additional information can be used to more appropriately guide medical management.

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