Comparing the Prognostic Utility of the CCP Score for Predicting Metastatic Disease in African American and Non-African American Men with Prostate Cancer

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BACKGROUND

- The cell cycle progression (CCP) score is based on measuring the expression levels of CCP genes and has proven to be a robust predictor of prostate cancer outcomes in various clinical settings and patient populations.[1]
- However, data regarding the ability to predict outcomes in African American men are sparse.[2]

OBJECTIVE

- Here, we evaluate the utility of the CCP score generated from diagnostic biopsy to predict metastatic disease in a large cohort of treated patients that is highly enriched with an African American patient population.

METHODS

COHORT

- This is a retrospective study of patients diagnosed with clinically localized adenocarcinoma of the prostate and treated at Ochsner Clinic (New Orleans, LA) between January 1, 2006 and December 31, 2011 with available biopsy FFPE sample.

MOLECULAR TESTING

- Samples were analyzed for the expression levels of 31 CCP genes and 15 housekeeper genes by quantitative RT-PCR.
- The CCP score was calculated as the unweighted average of the CCP gene expression normalized to the housekeeper gene expression.
- A combined clinical cell-cycle risk (CCR) score was calculated as 0.57 CCP + 0.37 CAPRA.[3]

STATISTICAL ANALYSIS

- Progression to metastatic disease was confirmed by imaging, and was evaluated in the entire cohort (39 events, 5.1%) and in the subset of men who received definitive therapy (28 events, 4.3%).
- Time to metastatic disease was measured in days from date of diagnosis. Outcome data was censored at 10-years.
- Statistical analysis was performed according to a pre-designed Statistical Analysis Plan.
- Race was coded as African American and non-African American.
- P-values are for the Cox partial likelihood ratio test statistic, comparing the full to the reduced model, i.e. the model with and without the variable of interest. The hazard ratio (HR) and 95% profile likelihood confidence intervals (CI) are reported.
- Wilcoxon rank sum statistic was used to compare distributions.

RESULTS

- 969 clinically eligible cases were submitted for molecular testing. 767 had passing CCP scores and complete clinical information for calculation of CAPRA.
  - 281/767 (36.6%) men in this cohort were African American.
  - 646/767 (84.2%) men received definitive treatment by radical prostatectomy (RP) or radiation.
- Comparisons of demographic and clinical characteristics by race were very similar with the following exceptions:
  - Median age-at-diagnosis: 66 years for non-African American vs 63 years for African American (p=0.00019).
  - Median PSA: 5.8 ng/mL for non-African American vs 6.9 ng/mL for African American (p=0.000038).
- The CCR score distribution was similar for African American and non-African American men (p=0.38; Figure 1).

Figure 1. Distribution of CCR scores by race

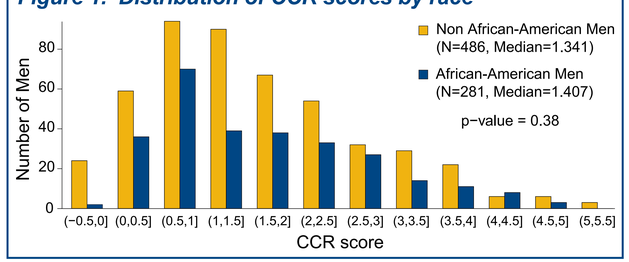
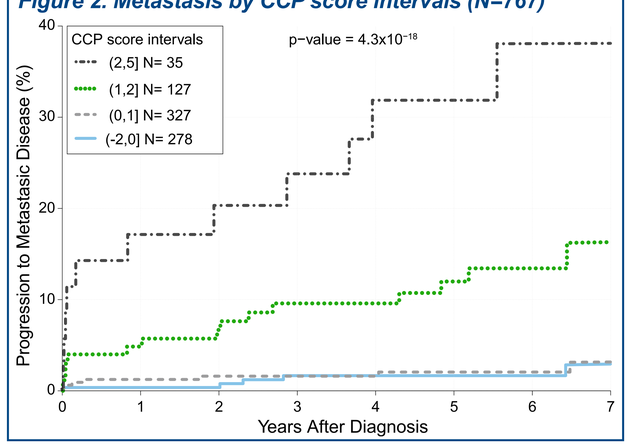


Figure 2. Metastasis by CCP score intervals (N=767)



- CCP score was a significant predictor of metastatic disease in univariate (HR per unit score = 2.76 (95% CI 2.09, 3.57), p=2.8x10^{-11}; Figure 2) and multivariate analysis (Figure 3, Table 1).
- The CCP HR per unit score was not significantly different by race (p=0.20), or treatment group (p=0.09) in the multivariable model.

Figure 3. Progression to metastasis (N=767)

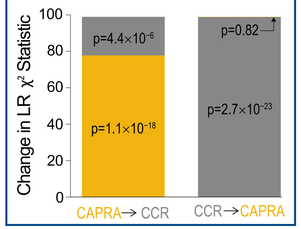
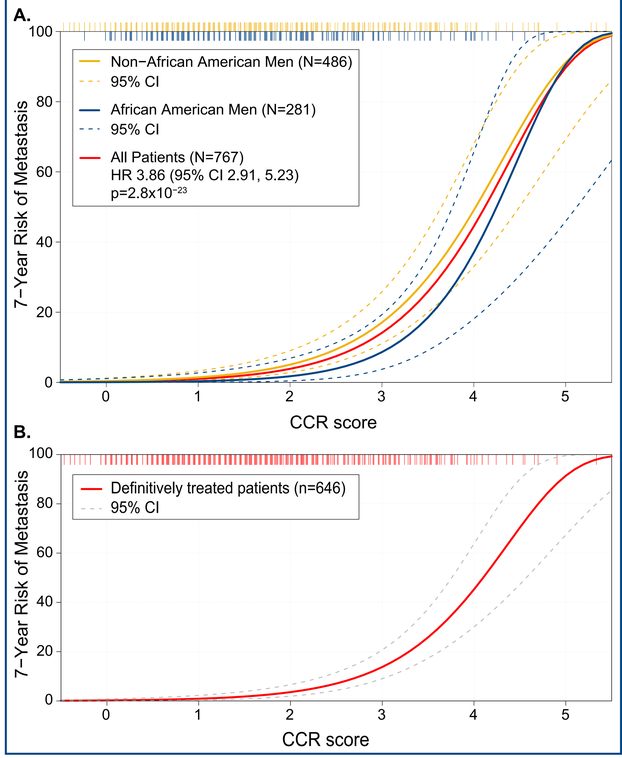


Table 1. Multivariable Cox model

Variable	HR (95% CI)	P-Value
Molecular and Clinical Scores		
CCP score	2.04 (1.47, 2.79)	3.4×10^{-5}
CAPRA score	1.72 (1.46, 2.03)	6.7×10^{-11}
Race		
African American/Non-African American	0.50 (0.22, 1.04)	0.063
Treatment		
Radiation/RP	2.90 (1.06, 7.87)	0.21
Radiation with adjuvant hormones/RP	1.00 (0.38, 2.73)	
Hormones only	1.73 (0.59, 5.14)	
Watchful Waiting	No Events	
Unknown	1.63 (0.09, 9.70)	

- CCR was highly predictive of metastatic disease in the entire cohort, and the estimated risk did not differ significantly by race (Figure 4A).
- The score was also highly prognostic in the subset of patients who had definitive therapy (Figure 4B).

Figure 4. 7-year predicted risk of metastasis (A) by race and (B) in men who had definitive treatment.



CONCLUSIONS

- Consistent with previous reports,[4] the CCP score was a strong predictor of metastatic disease in a large cohort that included a substantial proportion of African American patients.
- In this analysis, there was no evidence of an interaction between the CCP score and either race or treatment (i.e. the CCP HR was not significantly different).
- Contrary to expectation, this study provides no evidence that African American men have more aggressive disease than non-African American men after accounting for all available molecular and clinicopatholgic prognostic information.
- This study provides further validation that the CCP score provides significant and independent prognostic information about prostate cancer outcomes in all men irrespective of race, risk group, or treatment approach.

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