Evaluating the Impact of African American Ancestry among Men with Localized Prostate Cancer Treated with Radical Prostatectomy

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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 is sparse.[2]
- Prior data has suggested that African American men present with more aggressive disease compared to men of other ancestries.

OBJECTIVE

- Here, we examined the effects of ancestry on clinical and molecular measures of disease aggressiveness as well as long-term oncologic outcomes in men treated with radical prostatectomy (RP) for localized prostate cancer.

METHODS

COHORT

- Retrospective study of patients who were diagnosed with clinically localized adenocarcinoma of the prostate at Ochsner Clinic (New Orleans, LA) between January 1, 2006 and December 31, 2011.
- The subset of patients treated by RP was assessed here (384/767).

MOLECULAR TESTING

- Formalin−fixed paraffin embedded biopsy tissue was analyzed for the expression levels of 31 CCP genes and 15 housekeeper genes by quantitative RT-PCR. A CCP score was calculated as the normalized expression of the CCP genes.
- A combined clinical cell-cycle risk (CCR) score was calculated as 0.57 CCP + 0.37 CAPRA.[3]

STATISTICAL ANALYSIS

- Clinical (Gleason score, tumor stage, CAPRA score) and molecular (CCP score) measures of disease aggressiveness were compared based on ancestry (African American versus 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.
- Fisher's Exact Test and Wilcoxon Rank Sum Test were used to compare ancestries.

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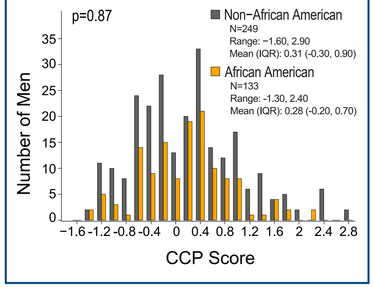
RESULTS

- 382 patients received definitive treatment by RP, had passing CCP scores, and had complete clinical information.
  - 133 of these patients were of African American ancestry.
- There were no significant differences in clinicopathologic features by ancestry, with the exception of PSA (Table 1).

Table 1. Clinical Characteristics by Ancestry

	Non-African American		African American		
Feature	**N**	**Median (IQR) or Frequency**	**N**	**Median (IQR) or Frequency**	**P-value**
Age at diagnosis	249	62 (57, 66)	133	61 (55, 64)	0.092
Pre-biopsy PSA, ng/μL	249	5.2 (4.1, 7.3)	133	5.8 (4.6, 8.3)	0.0087
% positive cores	249	41.7 (23.5, 66.7)	133	44.4 (33.0, 54.6)	0.55
Gleason Score (Diagnostic Biopsy)					
<7	140	56.2%	80	60.2%	0.26
3+4=7	58	23.2%	34	25.6%	
4+3=7	20	8.0%	5	3.8%	
>7	31	12.4%	14	10.5%	
Clinical T Stage					
T1	192	77.1%	111	83.5%	0.27
T2	54	21.7%	20	15.0%	
T3	3	1.2%	2	1.5%	
AUA Risk Category					
Low	124	49.8%	70	52.6%	0.78
Intermediate	83	33.3%	44	33.1%	
High	42	16.9%	19	14.3%	
CAPRA Risk Category					
Low (0-2)	125	50.2%	67	50.4%	0.76
Intermediate (3-5)	108	43.4%	55	41.4%	
High (6-10)	16	6.4%	11	8.3%	

Figure 1. Distribution of CCP Score by Ancestry



- There were no differences in the CCP score distributions according to ancestry (Figure 1).
- There was no significant difference in biochemical recurrance (BCR) according to ancestry (Figure 2, Table 3).
- CCP score was a significant predictor of BCR, regardless of ancestry (Figure 2).
- Only men of non−African American ancestry progressed to metastatic disease within the ten years of follow−up (Table 2).

Figure 2. Kaplan−Meier Plot for BCR

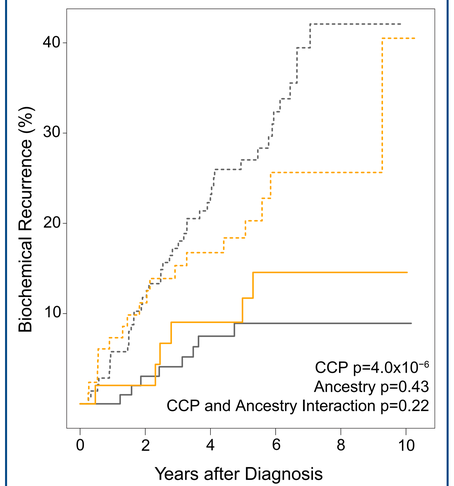


Table 3. Univariate and Multivariate Cox Models - BCR Endpoint (n=382; BCR events=75)

Variable	N	HR (95% CI)	P-Value
Univariate			
CCP score	382	1.73 (1.35, 2.21)	$1.28x10^{-5}$
CAPRA	382	1.50 (1.35, 1.67)	$1.49x10^{-14}$
Ancestry (AA/non-AA)	133/249	0.86 (0.53, 1.40)	0.55
Multivariate			
CCP score	382	1.46 (1.14, 1.87)	0.0040
CAPRA	382	1.47 (1.31, 1.64)	$1.16x10^{-9}$
Ancestry (AA/non-AA)	133/249	1.01 (0.62, 1.67)	0.96

CCR*Ancestry interaction p=0.057
AA=African American

- CCP score was a significant predictor of metastatic disease in univariate analysis (HR=3.07, 95% CI 1.50, 6.27; p=0.0013).

Table 2. Clinical Outcome and Follow-up Time by Ancestry

	Non-African American		African American		
Outcome	**event/N (%)**	**Median Follow-Up Time (IQR)***	**event/N (%)**	**Median Follow-Up Time (IQR)***	**P-value**
Biochemical recurrence	51/249 (20.5%)	5.6 (4.1, 6.8)	24/133 (18.0%)	5.8 (4.7, 7.4)	0.20
Progression to metastatic disease	9/249 (3.5%)	5.9 (4.4, 7.2)	0/133 (0.0%)	6.1 (4.9, 7.5)	0.13
Died of disease	2/249 (0.8%)	5.9 (4.4, 7.2)	0/133 (0.0%)	6.1 (4.9, 7.5)	0.16

*Men who had not experienced event and were alive at the end of follow-up

CONCLUSIONS

- Contrary to prior reports, the data appears to indicate that men of African American ancestry do not necessarily present with or develop a more biologically aggressive form of prostate cancer.
- Although the data represent only one institution's experience, it contains a highly robust African American population compared to prior reports.
- This study demonstrates that the CCP score was a robust and independent predictor of prostate cancer outcomes among men who had radical prostatectomy, regardless of ancestry.

REFERENCES

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