Prognostic Utility of Biopsy-Derived Cell Cycle Progression Score in Patients with NCCN Low-Risk Prostate Cancer Undergoing Radical Prostatectomy: Implications for Treatment Guidance

Jeffrey J. Tosoian, MD, MPH[1]; Meera R. Chappidi, MPH[1]; Jay T. Bishoff, MD[2]; Stephen J. Freedland, MD[3,4]; Julia E. Reid, MStat[5]; Michael K. Brawer, MD[5];Steven Stone, PhD[5]; Thorsten Scholomm, MD[6]; Ashley E. Ross, MD, PhD[1]

[1]The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine [2]Intermountain Urological Institute, Intermountain Health Care [3]Durham VA Medical Center
[4]Cedars-Sinai Medical Center [5]Myriad Genetics, Inc. [6]Institute for Pathology, University Medical Center Hamburg-Eppendorf

BACKGROUND

- Gleason score 6 prostate cancer represents a broad disease spectrum with optimal treatment varying widely from active surveillance (AS) to immediate curative therapy.[1]
- Characterizing the biologic aggressiveness of Gleason score 6 tumors has proven difficult, and clinical features alone are not enough to accurately stratify patient risk.
- Previous studies have demonstrated that the cell cycle progression (CCP) score measured in prostate biopsy specimens was predictive of several clinical outcomes.[2,3]
- It is currently unclear whether the CCP score improves clinical risk stratification within Gleason score 6 cancers and the subset of patients with National Comprehensive Cancer Network (NCCN) low-risk disease.

OBJECTIVE

- Determine the prognostic utility of the CCP score in men with NCCN low-risk disease who underwent radical prostatectomy (RP).

METHODS

COHORT

- Patients who underwent RP for Gleason score ≤ 6 prostate cancer at three institutions (Martini Clinic [MC], Durham Veterans Affairs Medical Center [DVA], and Intermountain Healthcare [IHC]) were identified.

MOLECULAR TESTING

- The CCP score was obtained from diagnostic (DVA, IHC) or simulated biopsies (MC).
- Samples were analyzed for the expression levels of 31 CCP genes and 15 housekeeping genes by quantitative RT-PCR.
- The CCP score is an un-weighted average of the CCP genes normalized by the average of housekeeping genes.

STATISTICAL ANALYSIS

- Primary outcome was biochemical recurrence (BCR, PSA ≥ 0.2 ng/mL) after RP.
- Prognostic utility of the CCP score was assessed using Kaplan-Meier analysis and multivariable Cox proportional hazards models in the subset of men meeting NCCN low-risk criteria and the overall cohort (all GS ≤ 6 prostate cancer patients).

RESULTS

- The final cohort included 236 patients who had passing CCP scores and complete clinical and pathological data. to calculate CAPRA (Table 1).
  - 188/236 (79.7%) patients met NCCN low-risk criteria.
  - The median CCP score was -0.15 (IQR -0.7–0.4) and 59.3% of the population had a low CCP score of ≤ 0.

Table 1. Demographic and Clinical Characteristics of the Overall Cohort

Variable	Category	Overall Cohort
Total Subjects		236
NCCN Low-Risk Subjects, N (%)		188 (79.7%)
Study Institution, N (%)	MC	83 (35.2%)
	DVA	76 (32.2%)
	IHC	77 (32.6%)
Age (years)	Median (IQR)	61.4 (57.0–65.7)
Clinical Stage, N (%)	T1c	164 (69.5%)
	T2a	58 (24.6%)
	≥ T2b	14 (5.9%)
PSA (ng/mL)	Median (IQR)	5.7 (4.4–7.8)
Percent cores positive	Median (IQR)	30 (16.7–45.5)
Percent cores positive, N (%)	0.1–25%	106 (44.9%)
	25.1–50%	103 (43.6%)
	50.1–100%	27 (11.4%)
CAPRA score	Median (IQR)	2 (1–3)
CAPRA score, N (%)	Low risk (0–2)	176 (74.6%)
	Intermediate risk (3–5)	59 (25.0%)
	High risk (6–10)	1 (0.4%)
CCP score	Median (IQR)	-0.15 (-0.7–0.4)
CCP score, N (%)	≤0	140 (59.3%)
	0.01–1	77 (32.6%)
	>1.0	19 (8.1%)
Follow-up (months)	Median (IQR)	73 (54–118)
	Median (IQR)*	81 (61–120)
Biochemical recurrence , N (%)		56 (23.7%)

*Among men who did not experience BCR

- Five-year BCR-free survival was highest for the low CCP score group (CCP ≤ 0) in the overall cohort (85.9%, p=0.027) and NCCN low-risk cohort (89.2%, p=0.041) (Figure 1 and Table 2).

Figure 1. Biochemical Recurrence-Free Survival Stratified by CCP Category in the Overall Cohort and the NCCN Low-Risk Cohort

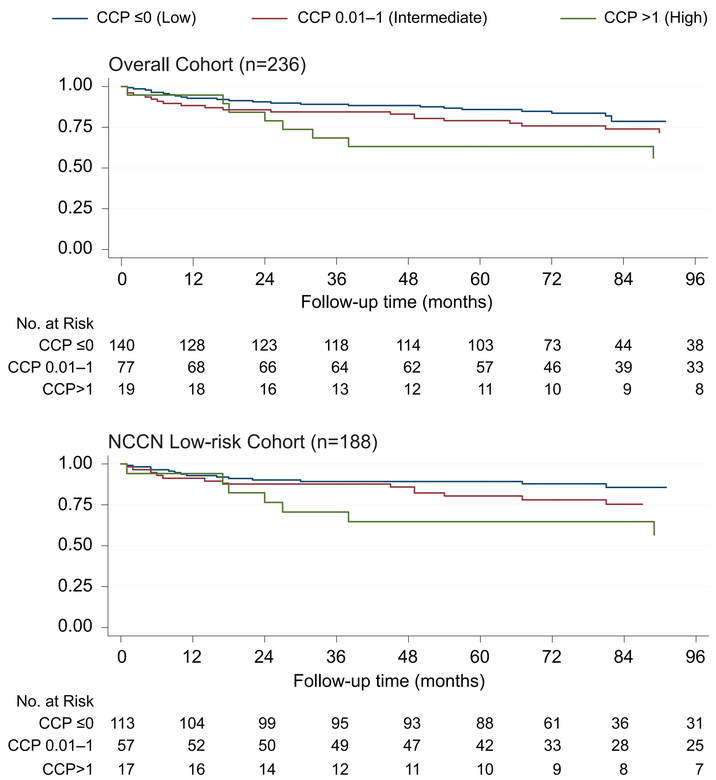

Table 2. Five-year freedom from BCR by CCP score category

Cohort	Low CCP ≤0	Intermediate CCP 0–1	High CCP >1
Overall (n=236)	85.9%	79.1%	63.1%
NCCN low-risk (n=188)	89.2%	80.4%	64.7%

- In multivariable models, the CCP score was an independent predictor of BCR in the overall cohort (p=0.039) and NCCN low-risk cohort (p=0.003) (Table 3).

Table 3. Univariable and multivariable Cox proportional hazards models to identify BCR predictors

Variable	Hazard Ratio (95% CI)	p-value
Overall Cohort (n=236)		
Univariable		
Age (per year)	1.03 (0.99–1.08)	0.150
PSA (per 1 unit)	1.05 (1.02–1.08)	0.00096
Percent positive cores	1.00 (0.98–1.01)	0.605
CAPRA score (per point)	1.42 (1.12–1.79)	0.0034
CCP score (per point)	1.46 (1.06–2.01)	0.020
Multivariable		
CAPRA score (per point)	1.39 (1.09–1.76)	0.0071
CCP score (per point)	1.41 (1.02–1.96)	0.039
NCCN Low-Risk Cohort (n=188)		
Univariable		
Age (per year)	1.03 (0.97–1.09)	0.319
PSA (per 1 unit)	1.35 (1.12–1.62)	0.0014
Percent positive cores	0.99 (0.98–1.01)	0.513
CAPRA score (per point)	1.16 (0.74–1.83)	0.508
CCP score (per point)	1.77 (1.23–2.56)	0.0022
Multivariable		
CAPRA score (per point)	1.02 (0.65–1.60)	0.939
CCP score (per point)	1.77 (1.21–2.58)	0.0030

CONCLUSIONS

- In NCCN low-risk patients, the CCP score improved clinical risk stratification of patients at increased risk of BCR.
- This suggests the CCP score could help improve the assessment of candidacy for active surveillance and guide optimal treatment selection in patients with NCCN low-risk prostate cancer.

REFERENCES

1. Mohler JL, et al. Prostate Cancer V3.2016. NCCN Clinical Practice Guidelines in Oncology. 2016.
2. Cuzick J, et al. *Br J Cancer.* 2012;106(6):1095.
3. Cuzick J, et al. *Br J Cancer.* 2015;113(3):382.

Presented at AUA May 13, 2017