Ability of cell cycle progression score to predict risk for progression to metastatic disease and disease-specific mortality in prostate cancer patients after prostatectomy

Gregory P. Swanson, MD1; Steven M. Stone, PhD2; Lauren H. Lenz, MS2; Todd Cohen, MD2

1. Baylor Scott and White Health, Temple, TX; 2. Myriad Genetics, Inc., Salt Lake City, UT

BACKGROUND

- Prostate cancer treatment aims to prevent metastatic disease (METS) and disease-specific mortality (DSM).
- A major challenge in treatment is identifying those at highest risk who would benefit from earlier intervention.
- Due to the long natural history of prostate cancer, defining prognostic factors associated with METS and DSM is difficult.
- This study, with over 20 years of follow-up, evaluates the prognostic utility of the cell cycle progression score (CCP) to predict METS and DSM after radical prostatectomy (RP).

METHODS

COHORT

- Eligiblity criteria:
- Prostate cancer treated with RP (1988-1997)
- Available tissue for CCP testing that resulted in a valid score
- Preoperative prostate-specific antigen (PSA)
- No neoadjuvant therapy
- Final study cohort included 360 men (Table 1).

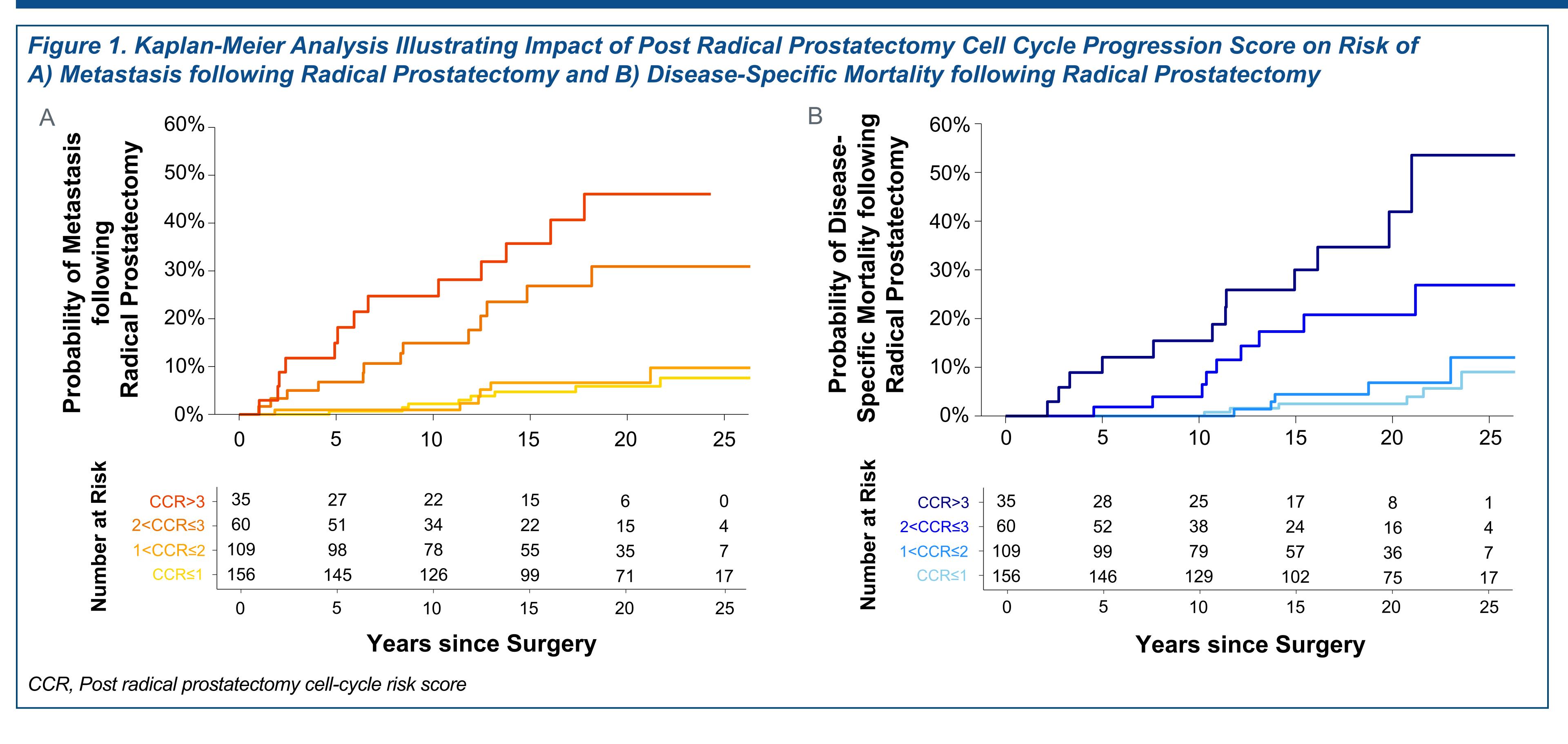
STATISTICAL ANALYSIS

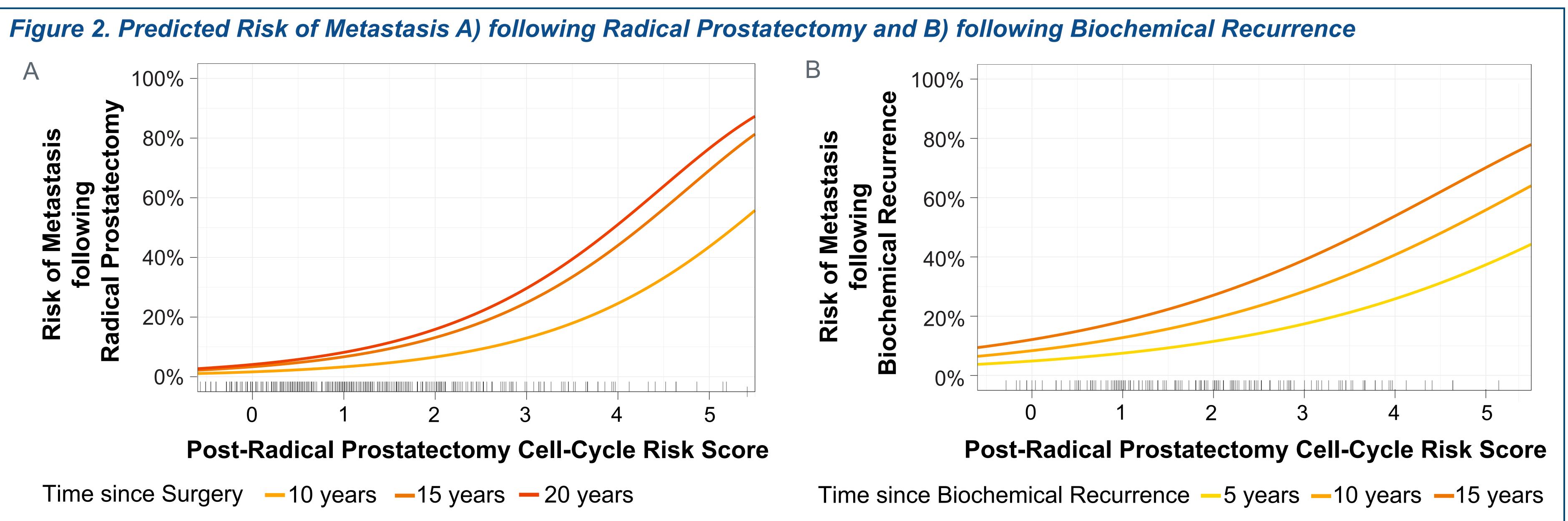
 Cancer of the prostate risk assessment post-surgical (CAPRA-S) was combined with CCP into a post-RP combined cell-cycle risk score (CCR = 0.38 × CAPRA-S + 0.57 × CCP).

Table 1. Patient Characteristics (N=360)

	Median (IQR) or N (%)		
Age at Surgery (years)	67.5 (63.3, 71.5)		
CAPRA-S	3 (1, 5)		
Low (0-2)	167 (46.4%)		
Intermediate (3-5)	126 (35.0%)		
High (6-12)	67 (18.6%)		
CCP	0.2 (-0.3, 0.7)		
Post-RP CCR	1.140 (0.494, 2.033)		
Below High-Risk Threshold (CCR ≤ 1.900)	260 (72.2%)		
Above High-Risk Threshold (CCR > 1.900)	100 (27.8%)		

RESULTS





- Median follow-up was 23.5 years for patients alive at last follow-up.
- Post-RP CCR was a significant predictor of metastasis [HR per unit score 2.03 (1.66, 2.48), p=2.1 × 10⁻¹⁰] (Figure 1A).
 - Post-RP CCR remained a highly significant predictor of METS after adjusting for CAPRA-S (p = 0.003), indicating that CCP provides significant prognostic information that is not captured by CAPRA-S.
- Post-RP CCR was highly prognostic of DSM [HR per unit score 2.11 (1.68, 2.65) p=1.7 ×10⁻⁹] (Figure 1B).
- Post-RP CCR remained significant after accounting for the information in CAPRA-S (p=0.004).
- Both CCP and post-RP CCR were also significant predictors of progression to METS after biochemical recurrence (BCR) (Table 2).
- Post-RP CCR was used to derive risk curves for progression to METS after RP (Figure 2A) and after BCR (Figure 2B).

Table 2. Predicting Time to Metastasis following Biochemical Recurrence

	HR (95% CI)	χ² Test Statistic	p-value	C-Index
Univariate				
CCP	1.75 (1.18, 2.59)	7.12	0.008	58.2%
CAPRA-S	1.16 (1.04, 1.29)	6.67	0.01	59.5%
Post-RP CCR	1.56 (1.20, 2.03)	10.91	0.001	62.8%
Multivariate				
CCP	1.70 (1.14, 2.53)	6.25	0.012	63.9%
CAPRA-S	1.15 (1.03, 1.28)	5.80	0.016	

CONCLUSIONS

- Overall, post-RP CCR significantly predicted METS and DSM in prostate cancer and was also highly prognostic in those with a post-RP rising PSA.
- Post-RP CCR is a useful tool for determining who is at higher risk of treatment failure and may benefit from earlier salvage intervention following RP.

Email questions to Gregory.Swanson@BSWHealth.org