Biopsy-Derived Cell Cycle Progression Score Outperforms Pathologic Upgrading or Upstaging in Predicting Biochemical Recurrence After Surgery

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BACKGROUND

- Active surveillance (AS) has gained rapid adoption for men with low-risk prostate cancer, but the risk of potential pathologic upgrading or upstaging remains a concern for many considering AS adoption.
- Prolaris is a prognostic RNA expression profile that has been shown to be a strong independent predictor of distal oncologic outcomes, and can be used to help identify AS candidates.
- In this study, for predicting biochemical recurrence (BCR), we compare biopsy-derived Prolaris to radical prostatectomy (RP) derived adverse pathology (upgrading or upstaging).

METHODS

- Cell cycle progression (CCP) testing was performed on biopsy specimens from a pooled cohort[1-2] of men with low-risk prostate cancer treated by RP.
- The CCP score was combined with the cancer of the prostate risk assessment (CAPRA) score using a validated algorithm to generate a clinical cell-cycle risk (CCR) score.
- The combined cohort included 557 men with clinical Gleason ≤ 3+4 and clinical Tstage ≤ T2[1-2].
- Adverse pathology was defined as patients with biopsy Gleason ≤ 3+4 and clinical stage ≤ T2 upgrading to a post-RP Gleason ≥ 4+3 and/or upstaging to post-RP pathological stage ≥ T3.
- Association with BCR was evaluated by Cox proportional hazards model stratified by site.

RESULTS

- In the pooled cohort, there were 56 (10%) men with adverse pathology and 116 (20%) with BCR.
- In multivariate analysis, CCP was strongly associated with BCR after adjusting for CAPRA and adverse pathology (Table 1).
- CCP score contributed more prognostic information to the final model than any other variable (Table 1).
- After adjusting for CAPRA, the LR χ^2 statistic for CCP is 2 times higher than that of adverse pathology in predicting BCR (Figure 1).
- CCR (a validated prognostic model for combining CCP and CAPRA) provides a greater significance (2.5X) for predicting BCR than adverse pathology alone (Table 1 and Figure 2).

Figure 1. Biochemical Recurrence Prediction After Adjusting for CAPRA

p-values for CCP and Adverse Pathology after adjusting for CAPRA

*as measured by LR χ^2

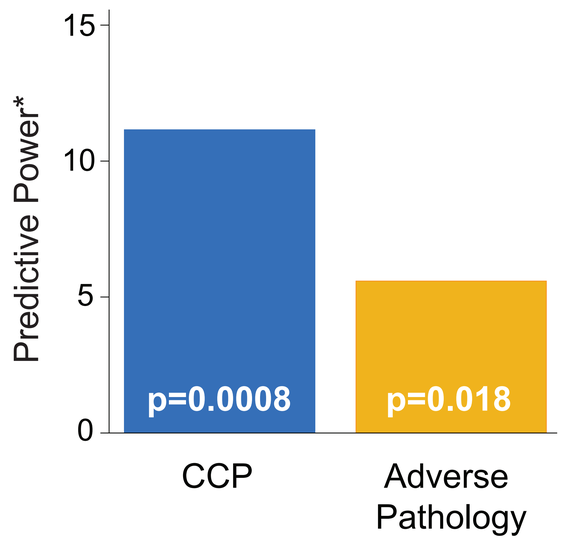

Figure 2. Biochemical Recurrence Prediction Difference Between CCR and Adverse Pathology

Univariate p-values for CCR and Adverse Pathology predicting BCR

*as measured by LR χ^2

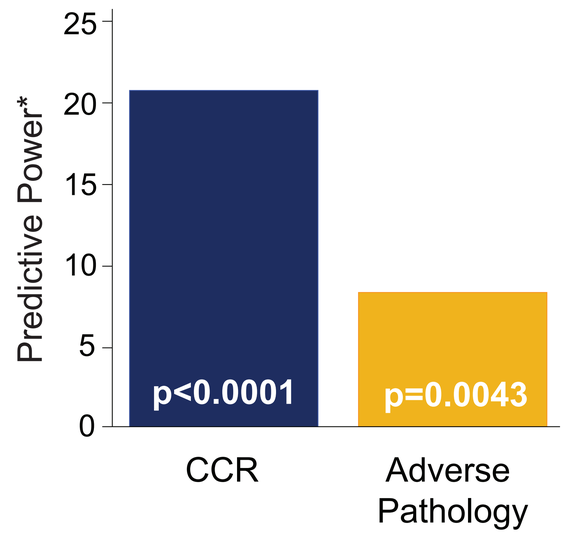

Table 1. Analysis of the Pooled Ochsner[1] and Bishoff[2] Cohort

Variable	Univariate HR (95% CI)	LR χ^2 value	Univariate p-value	Multivariate HR (95% CI)	LR χ^2 value	Multivariate p-value
CCP	1.53 (1.22, 1.92)	12.86	3.4×10^{-4}	1.47 (1.16, 1.86)	9.87	1.7×10^{-3}
CAPRA	1.27 (1.10, 1.46)	9.69	1.8×10^{-3}	1.21 (1.04, 1.41)	6.18	0.013
Adverse Pathology	2.07 (1.30, 3.29)	8.15	4.3×10^{-3}	1.68 (1.04, 2.70)	4.16	0.041
CCR	1.88 (1.44, 2.47)	20.65	5.5×10^{-6}	NA	NA	NA

All univariate and multivariate models are stratified by sites - Ochsner[1], Duke[2], and Martini Clinic[2].

CONCLUSIONS

- Within this pooled cohort, CCR has 2.5X the predictive power of adverse pathology.
- These data indicate that both CCR and CCP scores derived from the biopsy are better predictors of BCR than eventual adverse pathology, which can only be determined after surgery.

References: 1. Bardot, et. al., *J Urol*, 2017; 197(4):supplement e346 2. Bishoff, et. al., *J Urol*, 2014; 192(2):409-14

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