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

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BACKGROUND

- Potential pathologic upgrading or upstaging risk is a concern for many considering active surveillance (AS).
- Prolaris, a prognostic RNA expression profile, can independently predict distal oncologic outcomes and help identify AS candidates.
- We compared biopsy-derived Prolaris to radical prostatectomy (RP) derived adverse pathology (upgrading or upstaging) for predicting biochemical recurrence (BCR).

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 T stage ≤ 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).

Figure 1. LR χ2 for CCP is 2X higher than adverse pathology in predicting biochemical recurrence after adjusting for CAPRA.

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

*as measured by LR χ^2

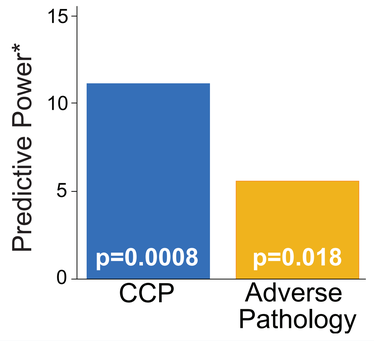

Figure 2. LR χ2 for CCR is 2.5X higher than adverse pathology in predicting biochemical recurrence in a univariate analysis.

Univariate p-values for CCR and Adverse Pathology predicting BCR

*as measured by LR χ^2

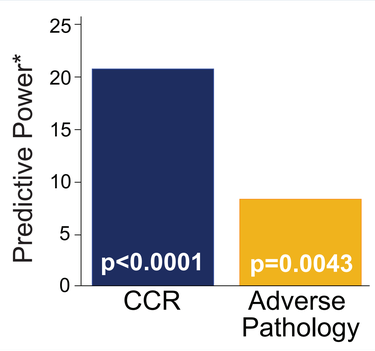

Table 1. Analysis of the Pooled Ochsner[1] and Bishoff[2] Cohort

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

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.

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References

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