18-874 - Comparison of cell cycle progression score with two immunohistochemical markers (PTEN and Ki-67) for predicting outcome in prostate cancer after radical prostatectomy

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Objectifs

-Previous studies of the cell cycle progression (CCP) score in surgical specimens of prostate cancer in patients treated by radical prostatectomy (RP) demonstrated significant association with time to biochemical recurrence (BCR).

-In this study, we compared the ability of the CCP score and the expression of PTEN or Ki-67 to predict BCR in a cohort of patients treated by RP.

-Finally, we constructed the best predictive model for BCR incorporating the biomarkers and relevant clinical variables.

Methods

The study population consisted of a retrospective cohort of prostate cancer patients who had RP surgery in French urological centers from 2000 to 2007.

The following clinical information was collected: age at surgery, pre-surgical measurement of PSA, pathological stage, whether the patient was treated with neoadjuvant therapy, date of RP surgery, date of BCR (if applicable), date of last follow-up, and the pathological measures required to calculate the CAPRA-S score

The CCP score is obtained by performing the Prolaris test

Results

- Among the 652 patients with CCP scores and complete clinical data, BCR events occurred in 41%, and time from surgery to last follow up among patients free of BCR was 72 months.
- In univariate Cox analysis, the continuous CCP score and positive Ki-67 predicted recurrence with an HR of 1.44 (95% CI: 1.17-1.75; p=5.3 x 10^{-4}) and 1.89 (95% CI: 1.38-2.57; p=1.6 x 10^{-4}), respectively.
- In contrast, PTEN expression wasn't associated with the risk of BCR. Of the 3 biomarkers, only the CCP score remained significantly associated in multivariable Cox model (p = 0.026).
- The best model incorporated CAPRA-S and CCP scores as predictors, with HR of 1.32 and 1.24, respectively.

TABLE 1: Clinical and pathological characteristics of the 512 patients with passing CCP scores and complete clinical data

Median age at surgery (IQR)	63 (58-67)
Median ng/ml pre-surgical PSA level (IQR)	8.0 (5.8-11.0)
No. pathological Gleason score (%)	
<7	184 (36%)
3+4	152 (30%)
4+3	140 (27%)
>7	36 (7%)
No. extra-capsular extension (%)	154 (30%)
No. seminal vesicle involvement (%)	35 (7%)
No. positive surgical margins (%)	39 (8%)
Median CAPRA-S score (IQR)	3 (1-4)
Median time in months from surgery to last follow-up among patients free of BCR (IQR)	72 (72-90)
No. BCR events (%)	211 (41%)
Median CCP score from RP (IQR)	0.08 (-0.36-0.57)
No. Ki-67 positive staining (%)	93 (18%)
No. PTEN negative staining (%)	53 (11%)

Abbreviations: CAPRA-S, Cancer of the Prostate Risk Assessment post-Surgical; IQR: inter-quartile range,

TABLE 2: Univariate Cox Proportional Hazards models of time from RP to BCR

	Number of patients (BCR events)	Hazard ratio	95% confidence interval	P-value
Age at surgery	512 (211)	1.02	0.99-1.04	0.19
Ln(1 + PSA)	512 (211)	1.40	1.02-1.91	0.036
Pathologic Gleason score				
<7	184 (57)	1.00 (ref)		$1.6x10^{-5}$
3+4	152 (66)	1.51	1.06-2.15	
4+3	140 (62)	1.60	1.12-2.30	
>7	36 (26)	3.51	2.20-5.59	
Extra capsular extension				
No	358 (127)	1.00 (ref)		$1.6x10^{-5}$
Yes	154 (84)	1.87	1.42-2.46	
Seminal Vesicle involvement				
No	477 (183)	1.00 (ref)	Ref	$9.0x10^{-7}$
Yes	35 (28)	3.16	2.12-4.71	
Positive surgical margins				
No	473 (180)	1.00 (ref)		$2.6x10^{-6}$
Yes	39 (31)	2.83	1.93-4.16	
CAPRA-S score	512 (211)	1.34	1.24-1.44	$6.3x10^{-14}$
CCP score	512 (211)	1.44	1.17-1.75	$5.3x10^{-4}$
Ki-67				
Negative	419 (157)	1.00 (ref)		$1.6x10^{-4}$
Positive	93 (54)	1.89	1.38-2.57	
PTEN				
Positive	421 (166)	1.00 (ref)		0.12
Negative	53 (27)	1.40	0.93-2.10	

TABLE 3 Multivariable Cox Proportional Hazards model of time from RP to BCR among patients with passing CCP scores, complete clinical data, PTEN and Ki-67 expression

Variable	Number of patients (events)	Hazard ratio	95% confidence interval	P-value
CCP score	474 (193)	1.28	(1.03, 1.59)	0.026
Ln(1 + PSA)	474 (193)	1.20	(0.85, 1.69)	0.299
Pathologic Gleason score				
<7	162 (50)	1.00 (ref)	ref	
3+4	144 (60)	1.18	(0.80, 1.73)	0.47
4+3	135 (60)	1.17	(0.73, 1.86)	
>7	33 (23)	1.74	(0.83, 3.69)	
Extra capsular extension				
No	325 (113)	1.00 (ref)	ref	0.024
Yes	149 (80)	1.45	(1.05, 1.99)	
Seminal vesicle involvement				
No	441 (167)	1.00 (ref)	ref	0.0012
Yes	33 (26)	2.21	(1.41, 3.46)	
Positive Margins				
No	438 (165)	1.00 (ref)	ref	$4.0x10^{-6}$
Yes	36 (28)	3.00	(1.98, 4.54)	
Ki-67				
Negative	386 (143)	1.00 (ref)	ref	0.32
Positive	88 (50)	1.30	(0.78, 2.16)	
PTEN				
Positive	421 (166)	1.00 (ref)	ref	0.46
Negative	53 (27)	1.17	(0.77, 1.79)	

TABLE 4 Best predictive Cox Proportional Hazards model of time to BCR considering molecular variables (CCP score, Ki-67, and PTEN expression) and post-surgical CAPRA-S score

Variable	Number of patients (events)	Hazard ratio	95% confidence interval	P-value
CCP score	512 (211)	1.24	1.01-1.52	0.040
CAPRA-S score	512 (211)	1.32	1.22-1.42	3.4x10-12

Conclusions

Our results show that the Prolaris test was a stronger predictor of BCR after RP compared to IHC markers, and that this test could be used in conjunction with the CAPRA-S score to better determine which RP patients are at highest risk of recurrence and need adjuvant treatment.